THESIS

FOR THE AWARD OF DEGREE OF

DOCTOR OF MEDICINE

SESSION 2020-2023

STUDY OF MICROALBUMINURIA AND ALBUMIN - CREATININE RATIO IN TYPE 2 DIABETES MELLITUS AND THEIR CORRELATION WITH GFR, ANTHROPOMETRY AND OTHER BIOCHEMICAL PARAMETERS.

By

DR. NIMISH KUMAR

SANTOSH DEEMED TO BE UNIVERSITY

NO. 1, SANTOSH NAGAR,

GHAZIABAD-201009, NCR DELHI, INDIA

DEPARTMENT OF GENERAL MEDICINE

SANTOSH MEDICAL COLLEGE & HOSPITAL

GHAZIABAD, NCR DELHI

SANTOSH
Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

COPYRIGHT CERTIFICATE - DECLARATION BY THE CANDIDATE

I hereby declare that Santosh Deemed to be University, Ghaziabad, (U.P.) shall have the right to preserve, use and disseminate this thesis titled **"Study of Microalbuminuria and Albumin - Creatinine Ratio in Type 2 Diabetes Mellitus and Their Correlation With GFR, Anthropometry and Other Biochemical Parameters"** in print or electronic format, for academic or research purpose.

Signature of Candidate

Date:

Place: Ghaziabad.

SANTOSH
Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

CERTIFICATE BY THE GUIDE

This is to certify that the thesis titled **"Study of Microalbuminuria and Albumin - Creatinine Ratio in Type 2 Diabetes Mellitus and Their Correlation With GFR, Anthropometry and Other Biochemical Parameters"** has been carried out by **Dr. Nimish Kumar** in partial fulfilment of the requirements for award of the degree of M.D. Medicine under my guidance and supervision and is completed to my full satisfaction.

DR. ASHOK KUMAR

MBBS, M.D
Professor & Head of Department,
Department of General Medicine,
Santosh Medical College & Hospital,
Ghaziabad – 201001 (U.P.)

SANTOSH
Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

CERTIFICATE BY THE CO-GUIDE

This is to certify that the thesis titled **"Study of Microalbuminuria and Albumin - Creatinine Ratio in Type 2 Diabetes Mellitus and Their Correlation With GFR, Anthropometry and Other Biochemical Parameters"** has been carried out by D**r. Nimish Kumar** in partial fulfilment of the requirements for award of the degree of M.D. Medicine.

DR. JUHI AGGARWAL

MBBS, MD
Professor and Head of Department,
Department of Biochemistry
Santosh Medical College & Hospital,
Ghaziabad – 201001 (U.P.)

SANTOSH
Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

CERTIFICATE BY HEAD OF THE DEPARTMENT

This is to certify that the thesis titled **"Study of Microalbuminuria and Albumin - Creatinine Ratio in Type 2 Diabetes Mellitus and Their Correlation With GFR, Anthropometry and Other Biochemical Parameters"** has been carried out by **Dr. Nimish Kumar** in partial fulfilment of the requirements for award of the degree of M.D. Medicine will be based on bonafide work carried out by him.

DR. ASHOK KUMAR

MBBS, M.D
Professor & Head of Department,
Department of General Medicine,
Santosh Medical College & Hospital,
Ghaziabad – 201001 (U.P.)

SANTOSH
Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

ENDORSEMENT BY THE DEAN OF THE COLLEGE

This is to certify that the thesis titled **"Study of Microalbuminuria and Albumin - Creatinine Ratio in Type 2 Diabetes Mellitus and Their Correlation With GFR, Anthropometry and Other Biochemical Parameters"** is a bonafide research work carried out by **Dr. Nimish Kumar** under the esteemed guidance of **Dr. Ashok Kumar,** Professor & Head of Department, Department of Medicine, Santosh Medical College & Hospital and is presented before the ethical committee of Santosh University, Ghaziabad for requisite approval.

DR. ALKA AGRAWAL
MBBS, MD
Dean
Faculty of Medical Sciences,
Santosh Medical College & Hospital,
Santosh Deemed to be University.
Ghaziabad-201001

SANTOSH
Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

ANTI-PLAGIARISM DECLARATION/UNDERTAKING

I, **Dr. Nimish Kumar**, hereby declare that the present thesis titled **"Study of Microalbuminuria and Albumin - Creatinine Ratio in Type 2 Diabetes Mellitus and Their Correlation With GFR, Anthropometry and Other Biochemical Parameters"** under the guidance of **Dr. Ashok Kumar** at Santosh Deemed to be University is a bonafide/original research work. I also hereby declare that there is less than 10% similarity and the present research work has not been submitted for the award of any degree/diploma of the same institution where the work was carried out or at any other institution.

Signature of the Guide **Signature of the Student**

I have verified the contents of the thesis and it has less than 10% similarity.

Dr. Jyoti Batra
Dean Research & Professor of Biochemistry
Santosh Medical College & Hospital
Santosh Deemed to be University
Ghaziabad – 201001(U.P.)

ACKNOWLEDGEMENT

The quest for knowledge and the burning desire in us is what drives and motivates us to explore new frontiers. At this juncture, it's time to acknowledged several individuals that have helped me a lot throughout my academic stint here at Santosh Medical College and Hospital, Ghaziabad.

Firstly, I would like to thank ***Dr. Alka Agrawal****, Dean, Faculty of Medical Sciences, Santosh Medical College & Hospital, Ghaziabad for providing me with all the resources and a golden opportunity to conduct the study in this prestigious institute. Her commitment to students is unrivalled and unwavering.*

I would also wish to express my gratitude to my guide ***Dr. Ashok Kumar****, Professor & Head of Department, Department of Medicine, Santosh Medical College & Hospital, Ghaziabad. His creative and logical thinking has greatly influenced me, which I admire and plan to emulate in the future. His commitment to students is unrivalled and unwavering.*

I am extremely grateful to my co guide ***Dr. Juhi Aggarwal****, Professor and HOD, Department of Biochemistry, Santosh Medical College & Hospital for her timely advice, constant support, able guidance and critical evaluation which aided in the timely completion of this dissertation.*

I would also like to extend my thanks and appreciation for all my Consultants ***Dr. Shivani Bansal, Dr. Ravi kumar, Dr. Ranjum Chaudhary, Dr Sonakshi Saxena, Dr Rashmi Mishra,*** *for their support and valuable comment. They also have been role models in many ways commendable with learning in every step of our journey in this institution thus leaving a lasting impression on our mind n souls.*

I would like to thank all my Seniors ***Dr. Abhay Singh, Dr Kandarp Patel, Dr Ananth, Dr Divyansh malik*** *this thesis could not have been completed without their help and support.*

My heartfelt thanks to my Colleagues ***Dr. Mahesh, Dr Surbhi thakur, Dr Jayesh Patil, Dr Laxmi Prasad, Dr Nitin Rana, Dr Abhishek Sharma, Dr Prabhjot Singh, Dr Mannat*** *who over these years have become like an extended family in a place far from home. With their help and support this journey has become memorable and easy sail thorough the tidy waves.*

*I would like to thank my juniors **Dr Krishna, Dr Swapnil, Dr Prasanth, Dr Lalit, Dr Nitesh, Dr Dewansh** this thesis could not have been completed without their help and support.*

I shall always cherish my association with Department of General Medicine, Santosh Medical College & Hospital, Ghaziabad where I had this opportunity of carrying out the present study and where I have learned and benefited immensely to become a good Physician.

*I owe a great debt to mother **Mrs. Punam Kumari** and my father **Mr. Satyendra Kumar**. I feel myself lucky, for having such caring understanding parents whose love and guidance throughout my life has shown me the right path, motivate me to work hard and achieve the goals when I felt disheartened or lost and to cherish every big and small achievements in this exceptionally enlightening phase of my small life. Their love and blessings always helped me and kept my dreams alive.*

*I owe a big thanks to my sister **Aprajita** for supporting all the time in preparing my thesis.*

No study can be completed without the co-operation of the patients involved and hence I express my sincere thanks and respect to all my patients from whom I have learned so much during this research. Their righteous feedbacks have been the true essence of my research.

Above all, I remember our divine GODs for giving me this opportunity, and blessing me with such empowering teachers, institution, intellect and skill in accomplishing this work as success.

Dr. Nimish Kumar
Batch – 2020-2023

TABLE OF CONTENTS

Sr. No.	TOPIC	Page No.
1	Introduction	1
2	Aim and Objectives	3
3	Review of Literature	4
4	Materials and Methods	23
5	Results	29
6	Discussion	44
7	Limitations	50
8	Conclusion	51
9	References	52
10	Annexures	61

LIST OF TABLES

Sr. No.	TITLE	Page No.
1	Albuminuria Categories according to KDIGO Classification.	11
2	Distribution of subjects as per their duration of diabetes.	29
3	Gender distribution of the subjects with respect to duration of diabetes.	30
4	Age group distribution of the subjects with respect to duration of diabetes.	31
5	Mean ± SD of baseline characteristics with respect to duration of diabetes.	32
6	Mean ± SD of anthropometric parameters with respect to duration of diabetes.	33
7	Presence of comorbidities in the respective study groups.	34
8	Mean ± SD of blood pressure parameters with respect to duration of diabetes.	35
9	Mean ± SD of laboratory parameters with respect to duration of diabetes.	36
10	Mean ± SD of lipid profile parameters with respect to duration of diabetes.	39
11	Incidence of Nephropathy observed in the patients of each group.	40
12	Statistical analysis of patient parameters with respect to duration of diabetes.	41
13	Multivariate linear regression analysis of all the variables w.r.t to uACR.	43
14	Correlation of parameters with uACR.	43

LIST OF GRAPHS

Sr. No.	TITLE	Page No.
1	Mean ± SD of the duration of diabetes in the respective group.	29
2	Distribution graph of the gender in the respective group.	30
3	Distribution graph of the age group in the respective group.	31
4	Box plot of the anthropometric parameters in the respective group.	33
5	Distribution graphs of comorbidities in the respective study groups.	34
6	Box plot of blood pressure parameters with respect to duration of diabetes.	35
7	Box plot of laboratory parameters with respect to duration of diabetes.	36
8	Box plot of microalbumin with respect to duration of diabetes.	37
9	Box plot of albumin-to-creatinine ratio with respect to duration of diabetes.	37
10	Box plot of eGFR with respect to duration of diabetes.	38
11	Box plot of cholesterol & triglyceride with respect to duration of diabetes.	39
12	Box plot of lipid molecules with respect to duration of diabetes.	40
13	Distribution graph of Nephropathy observed in the patients of each group.	41

LIST OF CHARTS

Sr. No.	TITLE	Page No.
1	Progression of nephropathy.	5
2	Complications in type II DM & Diabetic nephropathy.	6
3	Overview of the pathological pathways in diabetic nephropathy.	7
4	Risk Factors for Development and Progression of Diabetic Nephropathy.	8
5	Factors that influence the development of microalbuminuria.	10
6	Factors that affect measurement of urine albumin/creatinine.	12

INTRODUCTION

Diabetes mellitus (DM) is one of the primary risk factors for developing renal impairment globally. Type 1 and type 2 DM may lead to chronic complication of diabetic nephropathy (DN).[1] The development of microalbuminuria has been considered to be one of the first clinical signs of a classic course of diabetic nephropathy, which leads to macroalbuminuria and then to progressive loss of glomerular filtration rate (GFR) and eventually end-stage renal disease. Microalbuminuria is the preliminary clinically detectable stage of DN and an salient marker of the increase of cardiovascular diseases.[2] Approximately, one-third of diabetic patients develop microalbuminuria after 15 years of the onset of disease, whereas full nephropathy can develop in nearly half of the patients developing microalbuminuria.[3] Continuous macroalbuminuria forecasts deprivation of kidney function and, more importantly, interventions that reduce macroalbuminuria also slow the loss of glomerular filtration rate. Patients with microalbuminuria can be readily identified with spot urine collections.[4] Spot urine collections can be used to assess the albumin to creatinine ratio (ACR), which has been shown to be a simple and accurate way to assess microalbuminuria. Abnormal albumin levels in urine can be detected in 30% of patients diagnosed with type 2 DM and presence of protein in urine can speed up the development of the renal disorder and subsequently lead to end-stage renal failure. Some encouraging evidence has indicated that microalbuminuria is to a certain extent preventable.[5,6]

Estimated GFR (eGFR) remains an independent and significant predictor after adjustment for conventional risk factors including age, sex, duration of diabetes, smoking, obesity, blood pressure, and glycemic and lipid control, as well as presence of diabetic retinopathy. Moreover, research has also indicated that decreased eGFR rate is not only the predictor of renal function impairment, but also a predictor of diabetic neuropathy, diabetic retinopathy, and other diabetic-related complications.[7,8] Hence, the evaluation of eGFR rate is critical in diabetic patients. The estimated GFR (eGFR) using the abbreviated equation from the Modification of Diet in Renal Disease (MDRD) study has been suggested as the best validated means for transforming serum creatinine measurements into GFR in adults, using age, sex and ethnicity as surrogates for muscle mass.[9] Anthropometric measures including waist circumference (WC), body mass index (BMI), hip circumference (HC), waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) have been commonly used to predict the risk of diabetes. However, BMI does

not provide information on body fat distribution and WC does not consider intraindividual and ethnic differentiation in lean body mass, body shape and height. Considerable controversy still prevails as to which measure most accurately defines body fat distribution. Researches from different countries and ethnicities in the world demonstrated thatanthropometric measures have different predictive powers for diabetes and hypertension.[10]

Management of traditional risk factors such as hypertension, hyperlipidemia, and smoking to improve cardiovascular and renal outcomes continues to be important in patients with chronic kidney disease. There is, however, growing recognition that non-traditional risk factors such as increased urinary albumin excretion, microalbuminuria, elevated serum creatinine levels, and/or decreased hemoglobin levels may also be important in individuals with chronic kidney disease.[11] Clinical factors associated with albuminuria and low GFR may be common but could be independent. Hence, a better understanding of the prevalence of albuminuria and risk factors associated with albuminuria is need for the hour for further development of preventable strategies for DN. The UK Prospective Diabetes Study even demonstrated that 51% of patients who progressed to chronic renal failure had no preceding albuminuria.[12] However, the proportions of patients with low GFR among type 2 diabetic patients with normoal buminuric, microal buminuria or macroal buminuria remain uncertain, and few such data are available on Asian diabetic populations.

NEED FOR STUDY

This prospective observational study was designed in an attempt to evaluate the relationship between microal buminuria,albumin-creatinine ratio with other biochemical parameters in type 2 DM and to examine whether this relation differs from that of non-diabetics. With a growing adult population in our country, there is a need to study the extent of diabetic nephropathy in diabetic patients which not only helps in triage but will help us to effectively use the limited resources available in smaller centers which ultimately will guide the development of policies to reduce the burden of heart related ailments in India.

AIM AND OBJECTIVES

Aim:

To evaluate relationship between microalbuminuria, urine albumin-creatinine ratio, GFR, anthropometry with other biochemical parameters in type 2 DM.

Objectives:

- To study the relationship between microalbuminuria, ACR with GFR in type 2 diabetes mellitus.
- To study the relationship between microalbuminuria and ACR in type 2 diabetes mellitus.
- To study the relationship between microalbuminuria, ACR with duration of diabetes mellitus.
- To study the relationship between microalbuminuria, ACR with HB1Ac in type 2 DM.

REVIEW OF LITERATURE

Due to various lifestyle modifications and other causes, metabolic disorders are on the rise in developing countries such as India. Additionally, it may increase the risk of acute coronary syndrome, cerebrovascular disease, neurodegenerative disease and other miscellaneous disorders. A large part of this increase is expected to derive from low-income, underdeveloped, and developing countries such as South Asian countries, Sub-African countries, Latin America, and some parts of the Middle East.[13] Assessment of renal function in individuals with diabetes mellitus (DM) is extremely important since diabetic nephropathy (DN) constitutes a major cause of chronic kidney disease in the world, which makes DM the most common cause of end-stage renal disease. This review of literature is carried out in lieu of better understanding the disease in itself by reviewing its pathogenesis, risk factors, complications, use of eGFR and its various calculation methods through means of published research over the time. The articles were shortlistedto provide new data, and cross-referencing was done to obtain insight into previous trends. The manual searched for related literature was also carried out from journals in the institutional library. The keywords used were: Diabetes, albuminuria, proteinuria, renal function, End Stage Renal Disorder, Glomeruli, Diabetic Nephropathy, etc.

Diabetic Nephropathy

Diabetic nephropathy (DN) or diabetic kidney disease is a disorder marked by the appearance of pathological quantities of urine albumin loss, diabetic glomerular injury, and reduction of glomerular filtration rate (GFR) in diabetics.[2] Diabetic nephropathy, especially related to type 2 diabetes, has become the single most important cause of ESRD worldwide. DN is marked by structural and functional changes. The glomeruli shows mesangial expansion, thickening of the basement membrane and, nodular glomerulosclerosis (Kimmelstiel–Wilson nodules). In early diabetic nephropathy, tubular hypertrophy is present but in due course interstitial fibrosis with tubular atrophy begins and arteriolar hyalinosis occurs. In advanced cases, there is an infiltrate of macrophages and T-lymphocytes. Histologically, there is podocyte loss and reduced endothelial cell fenestration. Functionally, there is early glomerular hyperfiltration and increased albuminexcretion; and with advancing nephropathy, increasing proteinuria and

declining GFR. A brief description of the functional and cellular pathology is provided below. Although it is conceptually easier to describe these pathways individually, these pathways overlap and interact with one another in vivo, and enhance one another's biophysiological effects.[14,15]

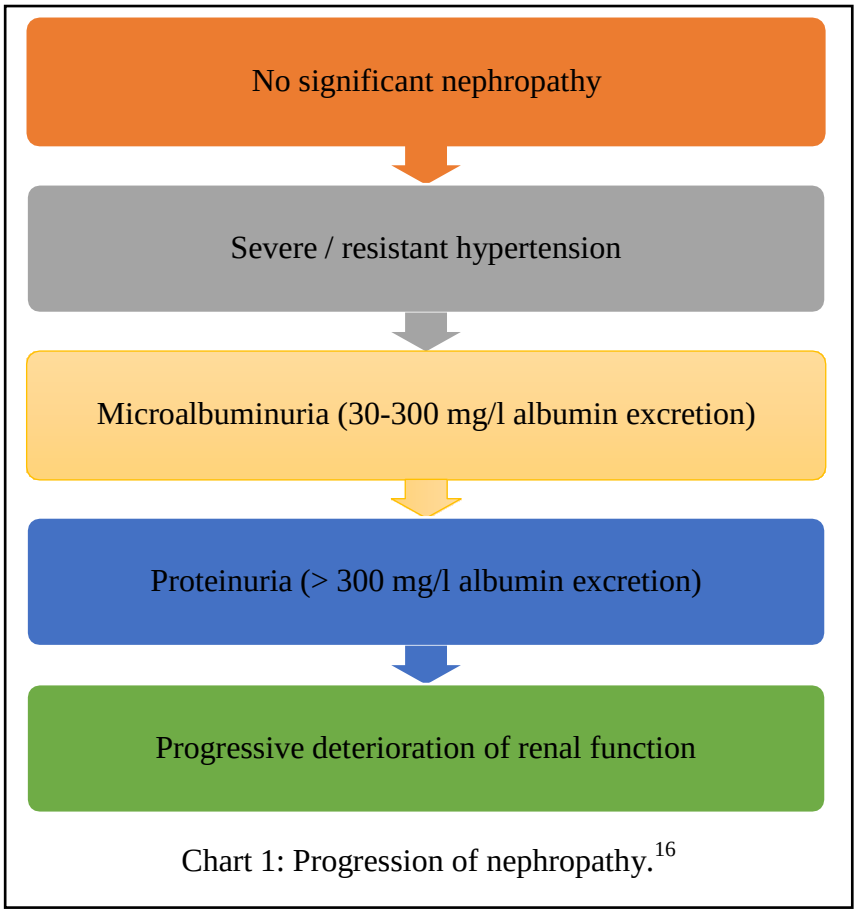

No significant nephropathy
Severe / resistant hypertension
Microalbuminuria (30-300 mg/l albumin excretion)
Proteinuria (> 300 mg/l albumin excretion)
Progressive deterioration of renal function

Chart 1: Progression of nephropathy.[16]

Not all diabetics develop DN and in those who do, progression is variable. The two main risk factors for diabetic nephropathy are hyperglycemia and arterial hypertension, but the genetic susceptibility in both type 1 and type 2 diabetes is of great importance. Other risk factors are smoking, dyslipidemia, proteinuria, glomerular hyperfiltration and dietary factors.[17]

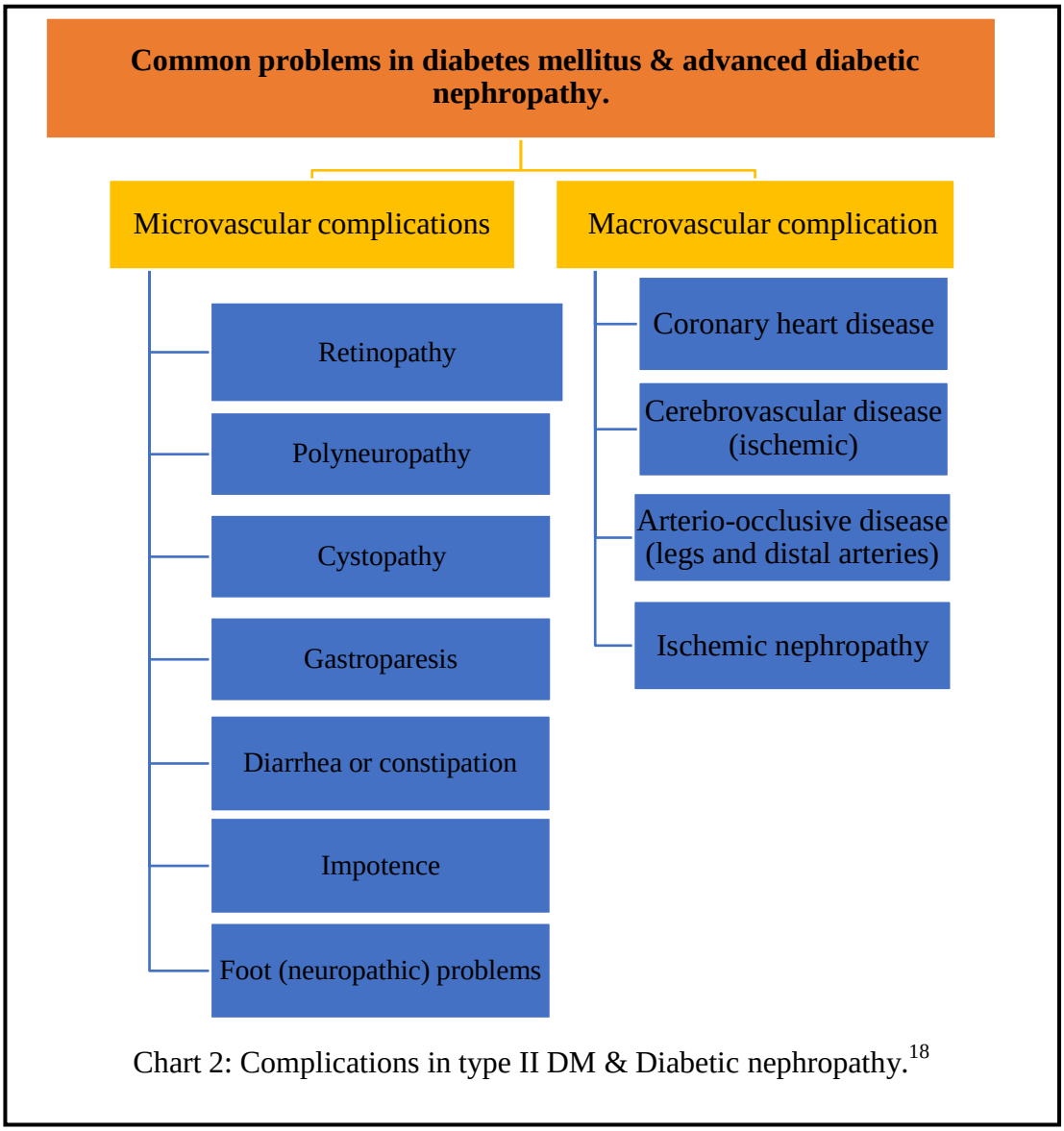


Chart 2: Complications in type II DM & Diabetic nephropathy.[18]

Pathophysiology

DN is characterized by structural and functional changes. In glomeruli, there is mesangial expansion, thickening of the basement membrane, and, characteristically, nodular glomerulosclerosis (Kimmelstiel–Wilson nodules). In early DN, tubular hypertrophy is present but eventually interstitial fibrosis with tubular atrophy develops, along with arteriolar hyalinosis. In advanced cases, there is an infiltrate of macrophages and T-lymphocytes. Histologically, there is podocyte loss and reduced endothelial cell fenestration.[19] Functionally, there is early glomerular hyperfiltration and increased albumin excretion; and with advancing nephropathy, increasing proteinuria and declining

GFR. A brief description of the functional and cellular pathology is provided below. Although it is conceptually easier to describe these pathways individually, these pathways overlap and interact with one another in vivo, and enhance one another's biophysiological effects.

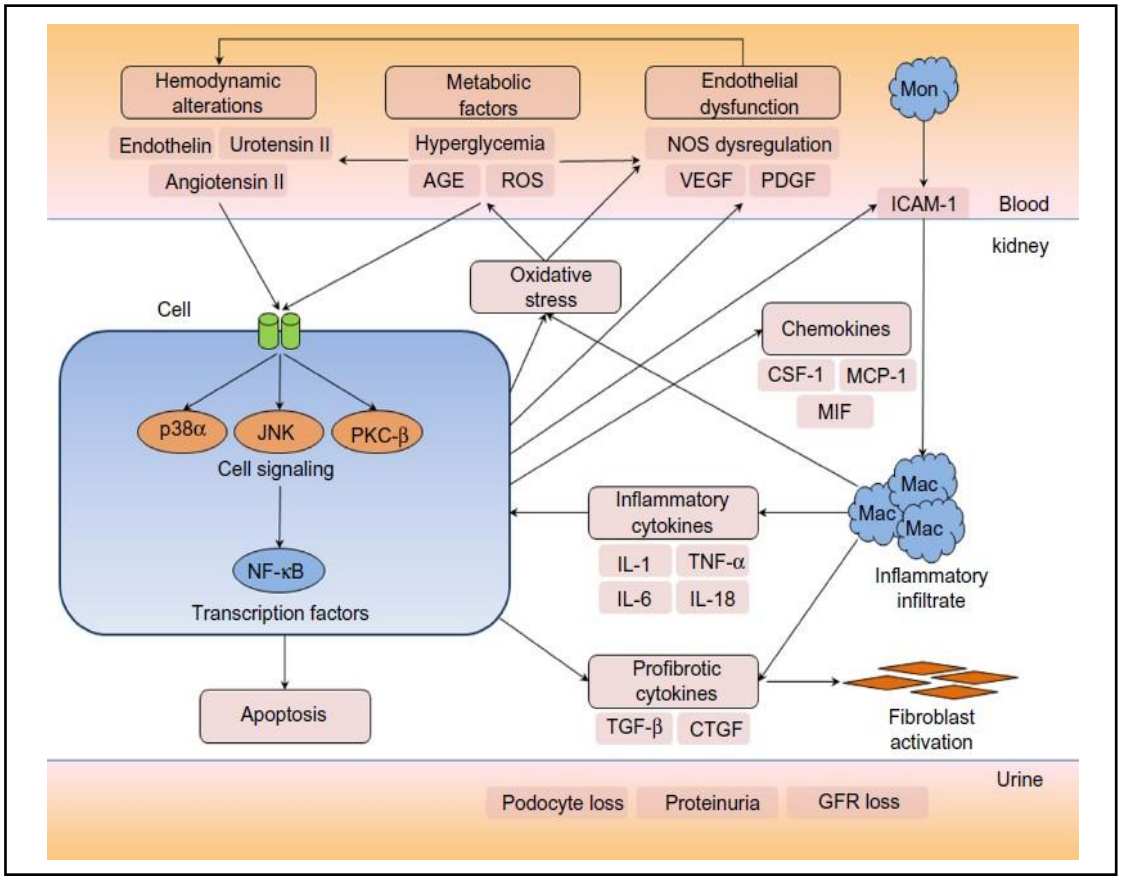


Chart 3: Overview of the pathological pathways in diabetic nephropathy.[20]

Risk Factors for Development and Progression of Diabetic Nephropathy:

Hypertension:

Hypertension is much more common amongst diabetic patients than in the general population and has been identified as a major risk factor for both macrovascular and microvascular complications including diabetic nephropathy. Total cardiovascular mortality in diabetes is strongly associated with raised blood pressure, particularly in type 2 disease.

Hypertension is strongly associated with insulin resistance, even in the absence of diabetes, and some 40-70% of type 2 patients will become hypertensive during their disease.[21] Only 25% of patients with type 1 diabetes are hypertensive and many of these will already have microalbuminuria or overt nephropathy.[22]

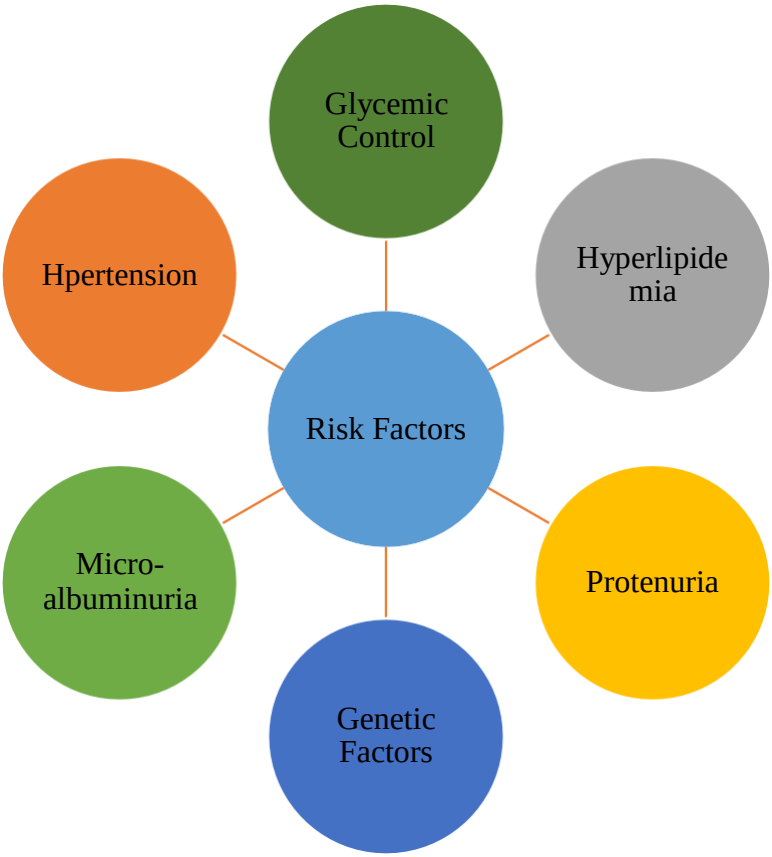


Chart 4: Risk Factors for Development and Progression of Diabetic Nephropathy.

Glycemic control:

Type 1 and type 2 diabetes have in common the state of chronic hyperglycemia, and glucose-dependent processes are likely to be involved in the pathogenesis of diabetic complications, including nephropathy. Glucose-induced tissue injury may be mediated by the generation of advanced glycated proteins or via other mechanisms such as the polyol pathway, both of which have been implicated in nephropathy.[22]

Proteinuria

Proteinuria is a broad term used to describe protein in the urine. Persistent proteinuria is a marker of kidney damage.[23] Proteinuria is a hallmark of diabetic nephropathy, microalbuminuria is the principal early predictor for progression of diabetic

glomerulopathy, and proteinuria may be viewed as a measure of the severity and promoter of progression of nephropathy.[24]

Genetic factors:

Genetic factors are likely to be important in diabetic nephropathy and the genetic basis of renal complication in diabetes is heterogeneous suggesting that the contribution from individual genetic factors is modest. Human studies have evidenced that renin–angiotensin–aldosterone system (RAAS) has a crucial role in diabetic kidney disease, with special attention has been focused on angiotensin-converting enzyme (ACE) gene, encoding a key enzyme in the RAAS that catalyses the conversion of angiotensin I to angiotensin II.[25-27]

Hyperlipidemia:

Hyperlipidemia is common in both type 1 and type 2 diabetes. Raised plasma triglycerides and low levels of high density lipoproteins (HDL) have been correlated with the development of diabetic nephropathy as well as with cardiovascular diabetic complications.[28]

Microalbuminuria:

If the amount of urine albumin exceeds 30 mg/d and is less than 300mg/d is called as **microalbuminuria**. The importance of microalbuminuria as an independent predictor of progressive renal disease and cardiovascular mortality was there after realized in a number of prospective and epidemiological studies particularly in patients with diabetes and hypertension.[29,30] Microalbuminuria precedes **macroalbuminuria** by an interval of 5 to 10 years. In patients with type 1 diabetes mellitus, renal function measured by GFR or creatinine clearance starts to decline with the onset of macroalbuminuria. However, in patients with type 2 diabetes mellitus, GFR may start to decline even in the microalbuminuria range.[31] In patients with overt nephropathy and type 1 diabetes mellitus, the effectiveness of antihypertensive therapy in reducing AER over the first 6 months of therapy is reflected in the subsequent rate of decline of GFR up to 5 years later.[32] That is, greater initial declines in albumin excretion are reflected in a lesser subsequent rate of decline of GFR. Similar evidence has been obtained in patients with non-diabetic renal disease.[33] Although it has been suggested that a reduction in microalbuminuria alone should be targeted as an endpoint, it is not known whether treatment of microalbuminuria per se, independent of blood pressure reduction, can prevent a subsequent decline in renal function in type 2 diabetes mellitus, since most

published studies are of less than 5 years duration.[34,35]

Chart 5: Factors that influence the development of microalbuminuria.[36]

- Increased body mass index
- Elevated blood pressure (systolic, diastolic, mean)
- Endothelial dysfunction
- Decrease in high-density lipoprotein levels
- Insulin resistance (hyperinsulinemia)
- Smoking
- Salt sensitivity
- Increased age
- DD ACE-genotype

Several methods can be used for detection of microalbuminuria. The urinary albumin/creatinine ratio (ACR) can be determined from a random, or preferably early morning, urine sample. This is often the easiest test in the setting of primary care and provides a practical screening method less prone to patient error than timed collection. The albumin excretion rate (AER) is more precise and can be measured formally from any timed collection, most commonly overnight (8 hours)—which is technically easier for the patient than a 24-hour collection. Microalbuminuria should be diagnosed on the basis of three positive tests—ACR, AER or a combination of the two—over a 3 to 6-month period.[22]

Table 1: Albuminuria Categories according to KDIGO Classification.[37]

Categories	Normal to Mildly Increased (A1)	Moderately Increased (A2)	Severely Increased (A3)
AER			
µg/min	<20	20–200	>200
mg/24 hours	<30	30–300	>300
ACR			
mg/g	<30	30–299	>300
mg/mmol	<3	3–30	>30

Clinical studies in adults and children have used 24-h, overnight urine collections and spot urine testing to estimate UAE (Urine albumin excretion). Timed urine collections are generally more cumbersome in the pediatric population compared to spot urine testing for estimation for UAE. Simple alternatives include estimation of urine albumin concentration or albumin creatinine ratio estimated from spot urine samples. An albumin-to-creatinine ratio >10 mg/g is diagnostic of microalbuminuria and is shown to be superior to urine albumin concentration and comparable to 24-h urine collections.[38]

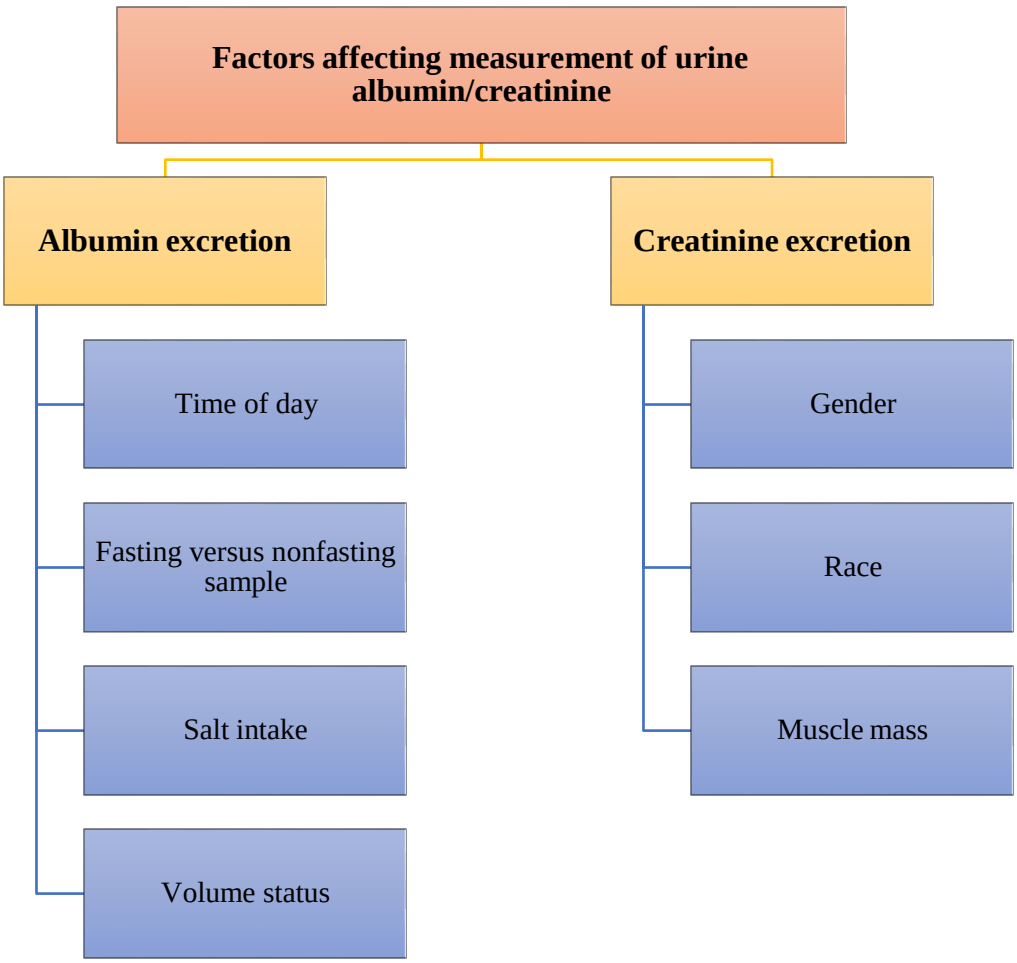


Chart 6: Factors that affect measurement of urine albumin/creatinine.[36]

In adults the use of the albumin-to creatinine ratio particularly in the general population has been validated in a number of epidemiological studies whereas in children there is relative paucity of such studies.[39-41] Due to a wider range of variation in UAE in children even within the normal range, it is recommended that the test should be repeated three times annually in diabetic subjects. Since, UAE is affected by exercise and time of the day, early morning urine sample for the albumin creatinine ratio provides a more sensitive estimate of microalbuminuria.[42] UAE is estimated to be the lowest in children<6 years old, followed by an increase through the adolescent years and a peak at age 15–16 years.[43] Female gender, Tanner stage 4–5 of puberty, height, and weight are all factors associated with a higher albumin excretion rate in healthy children.[44]

Symptoms:

Microalbuminuria, in itself, has not been associated with any specific symptoms. However, due to its link with diabetes, obesity, hypertension, and cardiovascular events, providers should focus on history and physical examination to assess for these complications. Specifically, paying attention to any personal or family history of renal, cardiac, and systemic diseases could reveal pertinent information. Additionally, patients with diabetes may present with symptoms of cardiac disease, vision difficulties, and urinary tract disorders. On physical exam, it is particularly important to evaluate for elevated blood pressure, abnormal cardiac exam, carotid pulse for bruits, and lower extremity swelling.[2] The majority of patients do not have any symptoms, and microalbuminuria is picked up on routine laboratory testing that is carried out to evaluate systemic diseases, such as diabetes mellitus or hypertension, or when a well-person examination is conducted.[45]

Evaluation:

The gold standard diagnostic test for the detection of microalbuminuria is a 24-hour urine collection as it has the lowest variability, but it is labor-intensive.[46] UACR corrects urine concentration and volume but can vary due to other factors. The urine spot collection changes depending on the urine volume. [47] Colorimetric dipstick test, in which random urine is taken as a sample. It is easy to perform and immediate result is obtained but less accurate and not a definitive test. Other alternatives are immunoturbidimetry, immunonephlometry, enzyme-linked immunosorbent assays, immunoassay with latex bodies, radial immunodiffusion, and fluroimmunoassay.[46] These are quantitative preferred methods which are more accurate but not immediate. Laboratory investigations should include a basic metabolic panel (to evaluate for decreased GFR, increased creatinine, and electrolyte imbalances) and a complete white count (for leukocytosis). Blood tests for the assessment of associated conditions are blood sugars, hemoglobin A1c, lipid panel, and troponins.[2]

Glomerular filtration rate

Glomerular filtration rate (GFR) represents the flow of plasma from the glomerulus into Bowman's space over a specified period and is the chief measure of kidney function. The kidneys receive 20% to 25% of the cardiac output (about 1.0 to 1.1 liters per minute) with the blood entering individual glomerular tufts via the afferent arteriole and exiting through the efferent arteriole.[48] The GFR is measured indirectly as the clearance of

exogenous filtration markers that are excreted by the kidney only by glomerular filtration. Clearance can be measured as either plasma or urinary clearance.[49]

Correlation with Diabetic Nephropathy:

Assessment of glomerular filtration rate is essential for clinical practice; it is crucial for deciphering the symptoms, signs, and laboratory abnormalities that might signify kidney disease, for drug dosing, and for detecting, managing and estimating the prognosis of DKD. Meta-analyses have shown that Impaired GFR and presence of albuminuria are independent risk factors for progressive DKD, ESRF, all-cause mortality and cardiovascular mortality in general population.[50] Therapeutic interventions can be implemented to ameliorate the onset and course of diabetic nephropathy significantly if the condition is recognized at its initial stages.[51] Thus, early and accurate detection of impaired GFR and albuminuria in diabetic patients is of upmost importance for initiating and optimizing treatment to slow down the progression of kidney failure, assessing and modifying other comorbid conditions, and reviewing prescription of renally excreted or nephrotoxic drugs.[52] High GFR, urinary albumin, and blood pressure along with low serum albumin and microangiopathy are other risk factors for reduced eGFR. Evaluation of eGFR is the best measure for the analysis of overall renal function. Decreased eGFR was observed among adults with DM compared to adults without DM.[53]

Estimation of GFR:

The most commonly used formulas to estimate glomerular filtration rate (eGFR) include the Modification of Diet in Renal Disease (MDRD) formula and the simplified MDRD 4 formula, both of which have been tested in diverse populations with reproducible results, as well as the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, which provides the most accurate GFR estimation (compared to a renal-clearance "gold standard") and is the formula advocated by contemporary consensus.[54] Creatinine clearance (CrCl) estimation can be performed by the Cockcroft–Gault (CG) formula. It should be emphasized that CrCl estimation by the CG formula comprises glomerular CrCl plus tubular CrCl, and therefore the overall CrCl may overestimate GFR by up to 40% in younger individuals without chronic kidney disease.[55]

The primary goal of a renal function estimation equation is to estimate GFR (and not tubular clearance). Therefore, for this purpose, the MDRD and CKD-EPI equations are suitable, whereas the CG/CG-BSA equations are not.[50,56]

Estimated GFR (eGFR) were calculated using the following equations:

1. Cockcroft-Gault ($eGFR_{CG}$) = [(140 − age) × weight (kg)]/SCr × 72 × [0.85 if female] and adjusted for body surface area of 1.73 m^2
    a. BSA calculated using the following DuBois formula, BSA = [weight (kg)] 0.425 × [height (cm)] 0.725 × 0.007184};
    b. GFR was calculated using the reexpressed four variable MDRD formula in which the constant 186 is replaced by 175. GFR = 175 × standardized $SCr^{-1.154}$ × $age^{-0.203}$ × 1.212 (if black) × 0.742 (if female); (standardized SCr—Recalibration of Scr methods to be traceable to the reference method for creatinine which is IDMS).[57,58]

The classical CG equation really predicts creatinine clearance, which exceeds glomerular filtration as a result of creatinine tubular secretion. In order to compensate for this effect, it has been recommended to introduce a correction factor in the classical CG equation.[59,60] The corrected CG equation improves the level of agreement with glomerular filtration and its level of agreement is slightly better than that for the MDRD equation.[59,61]

Previuos studies demonstrated that the decreased eGFR rate is not only the predictor of renal function impairment, but also a predictor of diabetic neuropathy, diabetic retinopathy, and other diabetic-related complications. Hence, the evaluation of eGFR rate is critical in diabetic patients and can be considered as a rational noninvasive mode of assessing the renal status in patients with type II DM.[62]

Is MDRD method less useful than CG ?

- In obese patients with established kidney disease, the Cockcroft-Gault equation overestimates GFR while underestimating GFR in lean subjects, possibly due to increasing weight; while performance of the MDRD equation in such patients is consistent regardless of weight. Bias of the Cockcroft-Gault formula was most pronounced in lean subjects, diminishing with increasing bodyweight.[63]
- In the Cockcroft-Gault equation, body weight is proportional to GFR; therefore, increasing body weight without a proportional increase in creatinine generation will tend to increase the estimation of GFR. However, weight is not included in the MDRD equation and therefore cannot influence performance.[64]

Lorenzo et al, found that the development of glomerular filtration rate < 60 mL/min per 1.73 m was associated with increased fasting insulin, triglycerides, free fatty acids, and uric acid and also with antihypertensive treatment, although not with waist circumference, controlling for age, sex, ethnicity, blood pressure, glucose, and C-reactive protein in

nondiabetic persons. This points towards the association of CKD with the risk of development of diabetes. James Sowers et al reviewed aspects of the association of diabetes with renal disease, emphasizing that albuminuria were associated with increased rates of cardiovascular disease (CVD) and mortality, and should be considered part of the cardiovascular risk factors in persons with diabetes.[65,66]

Albumin: creatinine ratio (ACR)

A urinary albumin-to-creatinine ratio (UACR) is a well-known marker of glomerular damage and therefore, one of the important diagnostic markers of chronic kidney disease.[67]**In Diabetic Nephropathy:**

The determination of the urinary albumin to creatinine ratio (UACR) using spot, first-morning urine sample is a simple and accurate test to quantify albuminuria. All patients with T2DM are recommended to test UACR levels annually in order to detect the occurrence of nephropathy.[68]

The albumin-to-creatinine ratio (ACR) in a single untimed urinary specimen is a reflection of urinary albumin excretion and is increasingly being accepted as a marker that predicts several important health outcomes, including hypertension, kidney failure, cardiovascular events, and mortality and associations have been observed throughout the biological range, even at levels far below those previously considered to be pathological (e.g., microalbuminuria)[69,70] The ACR is also closely linked to cardiometabolic risk factors, vascular disease, and insulin resistance and might therefore play a clinically important role in predicting future onset of diabetes. Observational studies have shown an association between ACR and other markers of urinary albumin excretion and incident diabetes.[71-73]

Anthropometry

The distribution of fat in the body is measured by using simple, most practical, at a low cost, and widely used markers of obesity index like anthropometric measurements, such as body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), and waist-to-height ratio (WHR).[74] It involves obtaining physical measurements of an individual and relating them to the standards. It is based on the concept that an appropriate measurement should reflect any morphological variation occurring due to significant functional physiological change. Body mass index (BMI) is the measurement most commonly recommended by national and international guidelines for the identification and treatment of obesity in adults, WC is an anthropometric measure also recommended

in the evaluation of the metabolic syndrome and to assess CHD risk. In 2009, more than 100 Indian medical experts representing reputed medical institutions, hospitals, government-funded research institutions, and policy-making bodies participated to develop Asian Indian-specific guidelines for defining and managing overweight and obesity.The consensus guidelines defined overweight as those with BMI between 23.0–24.9 kg/m^2 and obesity as those having BMI ≥ 25.0 kg/m^2.[75] Unfortunately, despite having clear cut Indian guidelines for defining overweight and obesity since 2009, the majority of contemporary studies and physicians in India are still using the international criteria for overweight and obesity. Majority still define obesity as BMI either ≥27.5 kg/m^2 (WHO 2004) or ≥30 kg/m^2 (WHO universal cut-off). This has serious health implications. This has led to many Indian individuals labelled as non-obese, despite being truly obese according to the consensus guidelines, thereby putting them at the risk of developing diseases associated with obesity.[75]

Anthropometric association with Diabetic Nephropathy:

Many studies to date have assessed the association of T2DM with anthropometric indices, bone mineral density (BMD), and body composition variables.[76] There are several possible explanations for the influence of the main disease risk factors in CKD, including DM and AH, being that the increase in BMI, and especially WC, are proportional to the increase in CKD. Secondly Overweight individuals have a more developed adipose tissue in their renal capsule, which compresses glomerular systems and tubular filtration, increasing the GFR and, consequently, increasing tubular sodium reabsorption. Body mass index (BMI), an anthropometric measure of whole-body adiposity has been associated with the development and Progression. High BMI and WC are major risk factors for DKD and DM since overweight and obesity are known to be predisposing to these diseases.[77] Ferreira ES et al. demonstrated that WC and lipid profile were associates with DM and DKD, being that the increase in VLDL-c increases the chances of the occurrence of DM and among diabetics, the WC and BMI index were higher when compared to individuals without DM.[78]

REVIEW OF RELATED LITERATURE

In this section, we will be reviewing the relevant studies pertaining to our topic and keeping the aim & objectives of our study at the centre point.

- **Karar et al.**[79] in 2015 studied on assessment of microalbuminuria and albumin creatinine ratio in patients with type 2 diabetes mellitus. The study included 100 male and female patients diagnosed with type 2 diabetes mellitus (DM) and excluding patients with type 1 DM. Increase in mean level of plasma creatinine (138 μmol/L), urine microalbuminuria (240 mg/L), albumin creatinine ratio (82) and HbA1c (8.7%) was observed among type 2 DM patients. Moderate positive correlation was observed between microalbuminuria and urine albumin creatinine ratio (r = 0.509 P = 0.0006) and between urine albumin creatinine ratio and plasma creatinine (r = 0.553 P = 0.017). The author concluded that type 2 DM patients who are at risk of developing renal impairment must be regularly monitored for microalbuminuria, urine albumin creatinine ratio, and HbA1c levels.

- **Idowu et al.**[80] in 2017 evaluated relationships between microalbuminuria and other predictors of morbidity and mortality in type 2 DM. Fifty type 2 diabetic subjects were recruited each for three groups separated by disease durations. Thirty non-diabetic subjects were recruited to control each group. Urine albumin-to-creatinine ratio (ACR) was estimated. Fasting plasma glucose (FPG), serum creatinine, total cholesterol (TC), triglycerides (TG), were measured. The diabetics with longest disease duration of >10 years were the oldest (65.86±1.71), had highest systolic BP (147.12±3.39mmHg) and least BMI (27.20±0.71Kg/m^2); they had poorest lipid control (TC:5.54±0.26mmol/L), though with the least TG (0.97±0.09mmol/L); they also had the most severe microalbuminuria (33.63±8.03g/L) and ACR (65.85±10.38mg/gm). Patients with diabetes of 5-10 years had the poorest glycemic control (FPG-7.82±0.47mmol/L; HbA1c-13.09±0.74%). Significant negative correlations exist between microalbuminuria, HbA1c (r=-2.28, p=0.028) and serum creatinine (r=-2.11, p=0.042) in patients with 5-10 years disease; a positive correlation between the ACR and TC (r=1.00, p<0.01) in those with >10 years disease. The author stated that the severity and progression of albuminuria are associated with longer duration of diabetes and poor glycemic control.

- **Chowta et al**.[81] in 2009 determined the correlation of microalbuminuria with age, sex, duration of diabetes, BMI, and creatinine clearance in type-2 diabetics in Indian population. One hundred patients (59 males and 41 females) with type-2 diabetes mellitus of duration six months or more and negative for albumin in urine by albustic method were included in the study. Overall, prevalence of microalbuminuria in the present study was 37%. Among 37 microalbuminuric patients, 9 patients had mild albuminuria, 18 had moderate albuminuria, and 10 had severe albuminuria. Mean BMI of microalbuminuric patients was 22.4 ± 6.9 kg/m2 and for normoalbuminuric patients it was 21.6 ± 4.2 kg/m2. The difference between the groups was not statistically significant. Mean duration of diabetes in microalbuminuric patients was 10.7 ± 5.0 years while in normoalbuminuric patients it was 3.2 ± 2.0 years, which was statistically highly significant. The serum creatinine clearance in the microalbuminuric (75.43 ± 20.57) and normoalbuminuric (83.24 ± 22.16) patients was found to be statistically insignificant. (P=0.08). Incidence of microalbuminuria increases with age as well as with increased duration of diabetes mellitus. There is no effect of BMI and sex on the prevalence of microalbuminuria in type-2 diabetes mellitus.

- **Efundem et al.**[82] in 2017 conducted a cross-sectional study on the prevalence and associations of microalbuminuria in proteinuria-negative patients with type 2 diabetes. A total of 162 type 2 diabetic patients were included. Using quantitative assessment, the prevalence of microalbuminuria was 14.2% whereas 26.5% had microalbuminuria with urine strip. In 28 participants [17.3% (95% CI 7.9–26.8%)], the eGFR was < 60 mL/min/1.73 m2. The mean BMI (29.8 ± 0.5 vs 27.6 ± 0.8) and mean eGFR in the normomicroalbuminuric group (101.3 ± 3.9 vs 46.5 ± 2.3) were higher when compared with the microalbuminuric group. The author concluded that microalbuminuria is associated with higher systolic and diastolic blood pressure, and declining kidney function. The results emphasized the urgent need to increase the accessibility to microalbuminuria testing to ensure that all diabetic patients with negative dipstick proteinuria can benefit.

- **Khadka et al.**[83] in 2018 had undertaken a study on the prevalence and Factors Associated with Microalbuminuria. Of 400 type 2 diabetic patients, 186 (46.5%) had microalbuminuria. The BMI of the patients without microalbuminuria (31.75±5.91 kg/m2) was less when compared to the patients with microalbuminuria (33.62±5.95 kg/m2). The mean duration of diabetes in patients without microalbuminuria

(3.66±2.44 years) was less when compared to the patients with microalbuminuria (7.36±3.70 years). The mean HbA1C in patients with (8.48±1.81) albuminuria and without albuminuria (7.84±1.93) was found to be statistically significant. (P=0.01). The mean microalbumin in patients with and without microalbuminuria was 11.15±6.11 mg/dl and 88.63±74.58mg/dL and it was found to be statistically significant. This study demonstrated that nearly half of the type 2 diabetic patients had microalbuminuria The results emphasized to increase to accessibility to microalbuminuria testing for all the type 2 diabetic patients and bring them under medical supervision to reduce the unwanted complications of diabetes mellitus.

- **Muddu et al.**[84] in 2019 studied the Utility of albumin to creatinine ratio in screening for microalbuminuria among newly diagnosed diabetic patients. Of the 175 patients recruited, males were 90(51.4%) and the mean age was 46±15 years. Majority of patients had type 2 DM 140 (80.0%) and the rest had type 1 DM 35 (20.0%). Mean glycated hemoglobin (HbA1C) was 13.9±5.3%. Mean duration of diabetes was 2 months. Prevalence of microalbuminuria was 47.4 % (95% CI: 40.0%-54.9%) overall. Among these patients, females had a higher prevalence of microalbuminuria, of 43.5% compared to males with 31.1%. Type 1 DM patients had a higher prevalence of microalbuminuria 19(54.3%) compared to 64(45.7%) among type 2 DM. Patients with central obesity as measured by waist hip ratio had a higher prevalence of Microalbuminuria of 57.7% compared to those without central obesity whose prevalence was 49.6%. Prevalence of microalbuminuria was high in this patient population of newly diagnosed diabetes mellitus. Early detection and management of microalbuminuria may help in preventing deterioration in renal function and development of overt diabetic nephropathy and progression to ESRD.

- **Dhonde S et al.**[85] in 2022 conducted a study of microalbuminuria in patients with type 2 diabetes mellitus. The overall prevalence of microalbuminuria is up to 35% in both type of diabetes; type 1 & type2. However, persons with type 2 DM exhibit the higher prevalence. Based on the duration of DM, 23% of patients had 5 years duration (group A), 56% of patients had more than 5-10 years of duration (group B) and 21% of patients had more than 10 years duration of DM (group C). The concentration of microalbumin (259.47 ± 89.95 mg/dl) was higher in patients in group c when compared to the patiens in group C (97.10 mg/dl, ≤ 5 years). The HbA1C (%) was less in group A (8.33 ± 1.52) when compared to group C (9.66 ± 1.49). There was a

significant difference in between the groups (P<0.004). When results of group B and group C were compared, there was a significant difference in the values of HbA1c (p< 0.000). Routine screening for microalbuminuria in type 2 diabetic patients will certainly, helpful for early detection of renal damage and thus to minimize the burdenof diabetic complications due to renal involvement.

- **Jatoi et al.**[86] in 2019 studied the prevalence of Microalbuminuria and Cardiovascular Risk Factors in Patients with Diabetes Mellitus Type-II. This was a retrospective cross-sectional and included 301 patients. the prevalence of microalbuminuria was found at 36.8%. The mean age was 57.8 ± 12.6 years, and females were 45%. The mean ± SD fasting blood glucose was 165.9 ± 71.9 mg/dL, while HbA1C% was 8.8 ± 5.6. Microalbuminuria was significantly associated with age, diabetes duration, systolic blood pressure, HbA1C%, fasting blood glucose, and triglyceride levels ($p \leq 0.05$). The author concluded that the microalbuminuria in T2DM patients was high in this study, which emphasizes the need for early detection of microalbuminuria.

- **Ritah Kiconci et al.**[87] in 2019 determined the prevalence of microalbuminuria in diabetic patients and established its association with traditional serum renal markers in assessment of incipient nephropathy. This was a cross-sectional study with140 participants with diabetes mellitus (DM). One hundred and nine participants (77.9%) had a family history of DM, and the average duration of DM was 6.8 years. Seventy percent of study participants had normal BMI with the average being 24.4 kg/m^2. Majority of the 140 study participants, 32 (22.9%), had microalbuminuria, 107 (76.4%) normoalbuminuria, and 1 (0.7%) macroalbuminuria. In addition, microalbuminuria was mostly detected among participants aged 45-54 years, 10 (24.4%), and the least affected age group was 18-34 years, 3 (23.1%). The author concluded that the prevalence of microalbuminuria in patients with diabetes in this study was high. The study suggests the need to screen for microalbuminuria early to reduce the possible burden of ESRD.

- **Daniel NH et al.**[88] in 2021 studied the anthropometric Measures and Incident Diabetic Nephropathy in Participants with Type 2 Diabetes Mellitus. Among the 8,887 participants with T2DM (5,489 men and 3,398 women), 5,296 participants (3,345 men and 1,951 women) developed the DN composite outcome during a follow-up period of 24302 person-years. The fully-adjusted HR for WC among

women was 1.35 (1.15-1.57) for the highest group (≥ 88cm), compared with the lower group (P-trend <0.001); the fully-adjusted HR for WHtR among women were 1.09, 1.12, and 1.14 for the 2nd to the 4th quartile compared with the 1st, respectively (P-trend = 0.047); also, the fully-adjusted HR for BMI among women were 1.28, 1.36, 1.43 and 1.32 for the overweight category to Class III obese category, compared with the normal weight category, respectively (P-trend = 0.035). Among women, however, higher levels of WC, WHtR, and BMI were all associated with an increased risk of doubling of SCr or > 20 mL/min/1.73m2 decrease in eGFR. The link between BMI and incident DN was stronger among participants with < 9years of diabetes duration than in those in ≥ 9years. Among men, higher levels of WC, WHtR, and BMI in the unadjusted models were associated with an increased risk of incident DN, but all lost significance in the full models although the 3rd quartile of WHtR showed marginally significant results (P = 0.052). Compared with the lowest quartile, the fully adjusted hazard ratio (HR) and 95% confidence interval (CI) for the 3rd quartile of WHtR was 1.10 among men. Among participants with T2DM, higher levels of both central and general obesity indexes were associated with DN risk among women but not in men.

MATERIALS AND METHODS

Type of Study & Study Site:

A hospital based cross-sectional observational study was undertaken to evaluate the relationship between microalbuminuria, albumin-creatinine ratio with other biochemical parameters in type 2 DM presented / referred to Santosh Medical College & Hospital, Ghaziabad (U.P.).

Study population:

The study population includes patients presented to Department of Medicine in the hospital; fulfilling the below mentioned inclusion and exclusion criteria.

Inclusion criteria:

1. Age group ≥ 18 years of either sex.
2. Patient with type II DM (as per American Diabetes Association).
3. Patient with written informed consent by patient/guardian.

Exclusion criteria:

1. Patients with type 1 diabetics.
2. Patients with hemolytic disorders.
3. Patients with urinary tract infections.
4. Patients with febrile illness.

Sample Size:

In this study, as we want to study the microalbuminuria and albumin-creatinine ratio in type 2 diabetes mellitus and their correlation with GFR and other biochemical parameters. Therefore, in order to calculate the sample size, we need to have the estimated prevalence

of type 2 diabetes mellitus as well as the prevalence of microalbuminuria in type 2 diabetes mellitus patients. To this reference, we have found that past researches have reported the prevalence of type 2 diabetes in India within a range of 1.9% to 25.2%.[89] For the sample size calculation, we will take the mid-range (or average) value of this range

i.e., 13.55%. Also, a research work also suggested that the prevalence of microalbuminuriain type 2 diabetes patients was 36.3%.[90] On calculating the sample size using these valuesand the formula given below:[91]

$$n_1 = \frac{\left[(Z_{\frac{\alpha}{2}}\sqrt{(r+1)\bar{p}\bar{q}} + Z_{1-\beta}\sqrt{(rp_1q_1 + p_2q_2)}\right]}{r(p_1 - p_2)^2}$$

And n_2=rn_1

Where

n_1= number of exposed

n_2= number of unexposed

$Z_{\alpha/2}$= standard normal deviate for two-tailed test based on alpha level (relates to the confidence interval level)

$Z_1-\beta$=standard normal deviate for one-tailed test based on beta level (relates to the power level)

r= ratio of unexposed to exposed

p_1= proportion of exposed with disease and q_1=1−p_1

p_2= proportion of unexposed with disease and q_2=1−p_2

$\bar{p}$= [p_1+rp_2] / r+1 and $\bar{q}$=1−$\bar{p}$

Sample Size: X-Sectional, Cohort, & Randomized Clinical Trials			
Two-sided significance level(1-alpha):			95
Power (1-beta, % chance of detecting):			80
Ratio of sample size, Unexposed/Exposed:			1
Percent of Unexposed with Outcome:			14
Percent of Exposed with Outcome:			36
Sample Size: X-Sectional, Cohort, & Randomized Clinical Trials			
Odds Ratio:			3.4
Risk/Prevalence Ratio:			2.6
Risk/Prevalence difference:			22
	Kelsey	**Fleiss**	**Fleiss with CC**
Sample Size - Exposed	61	60	69
Sample Size-Non-exposed	61	60	69
Total sample size:	122	120	138

Using the sample size calculated with Kelsey formula and adjusting it for loss to follow up cases as 20%, we get the final sample size of 150 patients. To make it more exclusive in terms of duration of diabetes, we would be dividing the 150 patients into three groups of 50 patients each.

Study Period:

The Study will be conducted for a period of one year from July 2021 to June 2022.

Method of Study:

A predesigned, self-administered proforma is designed keeping the objectives of the study at the Centre point. The purpose of the study was explained to the patient and informed consent will be obtained. Patients will be selected for study which satisfies all criteria. In the construction of the proforma, utmost care was taken to make it broad based, so that all the aspects desired to be studied could be incorporated in its body. Demographic

information of the participants studied, including age, sex, comorbidities and personal medical history were collected. Waist circumference was measured to the nearest 0.1 cm at expiration along a horizontal plane through the abdomen at the level of the midpoint between the lowest rib and the iliac crest. Body mass index was calculated as weight (kg) divided by the square of the height (m). Blood pressure was measured twice with the subjects in the sitting position after a 5-min rest. The lower value of two measurements will be used for the study. Clinical investigations such as complete blood count, erythrocyte sedimentation rate, urine tests (routine and microscopy), and glycosylated hemoglobin (HbA1c) and blood pressure were conducted. Proteinuria is defined as urine Albumin Creatinine Ratio (ACR) in a single spot urine sample.

- Normo-albuminuria < 30 mg/g.
- Microalbuminuria = 30-299 mg/g.
- Macroalbuminuria ≥ 300 mg/g.

HbA1C was measured by high-performance liquid chromatography. To diagnose Diabetic nephropathy, the level of albumin in urine was determined. To determine urine microalbumin (via immunoturbidimetry), a urine microalbumin excretion test was performed, and urine creatinine was determined using Jaffe's method. Serum creatinine was measured with Jaffe's method to calculate the eGFR. While eGFR was calculated using MDRD formula.

eGFR = 186× (SCR × 0.011) × (age) × (0.742, if female) × (1.210 if African American).

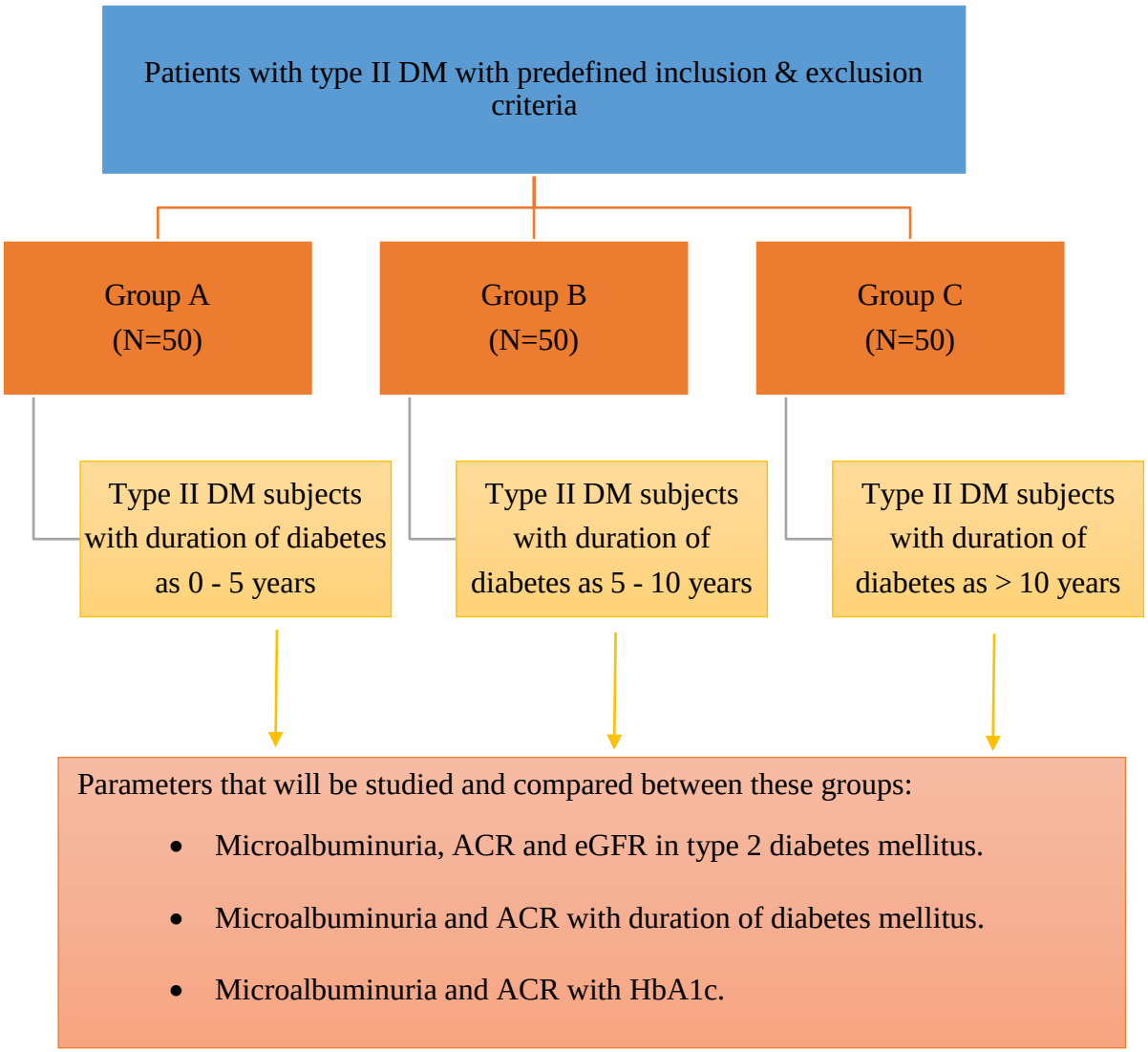
Subject Confidentiality:

Data collection was on paper. The patients participating in the study was contacted only by the persons involved in the study. All the patient specific data was kept in strict confidence. Patient identifiable data (name, contact, address, etc.) will not be presented in journal or any public forum.

Informed Consent:

Informed consent process was initiated prior to the individual agreeing to participate in the study and continuing throughout the individual's study participation. The form provided had all the information required for the patient to understand their role in the

study. It was in a language understandable by each member of the study population. It was submitted for the ethical committee clearance.


Patients with type II DM with predefined inclusion & exclusion criteria
Group A (N=50)
Group B (N=50)
Group C (N=50)
Type II DM subjects with duration of diabetes as 0 - 5 years
Type II DM subjects with duration of diabetes as 5 - 10 years
Type II DM subjects with duration of diabetes as > 10 years
Parameters that will be studied and compared between these groups:
Microalbuminuria, ACR and eGFR in type 2 diabetes mellitus.
Microalbuminuria and ACR with duration of diabetes mellitus.
Microalbuminuria and ACR with HbA1c.

Financial Inputs and Funding:

All the study related procedures and investigations was done according to the institutional protocol for the management of desired surgeries. All these expenses were borne by the patient. Also, this study was not being sponsored by any pharmaceutical company.

Ethical Considerations:

The protocol of the present study was submitted to the Ethics Committee of Santosh Medical College & Hospital for review. After getting their approval the study was initiated in the institution. Also prior to enrolling any patient in the study, a voluntary written informed consent was obtained for participation.

Statistical Analysis:

The data was collected using a predesigned template which was filled by the concerned physician involved in the immediate treatment of the patient. The collected data variables obtained was compiled by using an excel spreadsheet. Results are given as mean ± SD unless otherwise stated. After appropriate data filtration, the data sheet was transferred and analysed using Graphpad Prism (vs. 8.0). Statistical significance of the differences between the groups was determined by chi-squared tests for categorical variables and unpaired Student's t-test for continuous variables. Comparison of clinical variables among the groups was performed by one-way analysis of variance. Multiple logistic regression was used to describe the associations of variables with the presence of renal insufficiency and micro/macroalbuminuria.

Significant figures:

** Strongly significant (p value: $p \leq 0.01$)

* Moderately significant (p value: $0.01 < p \leq 0.05$)

+ Suggestive significance (p value: $0.05 < p < 0.10$)

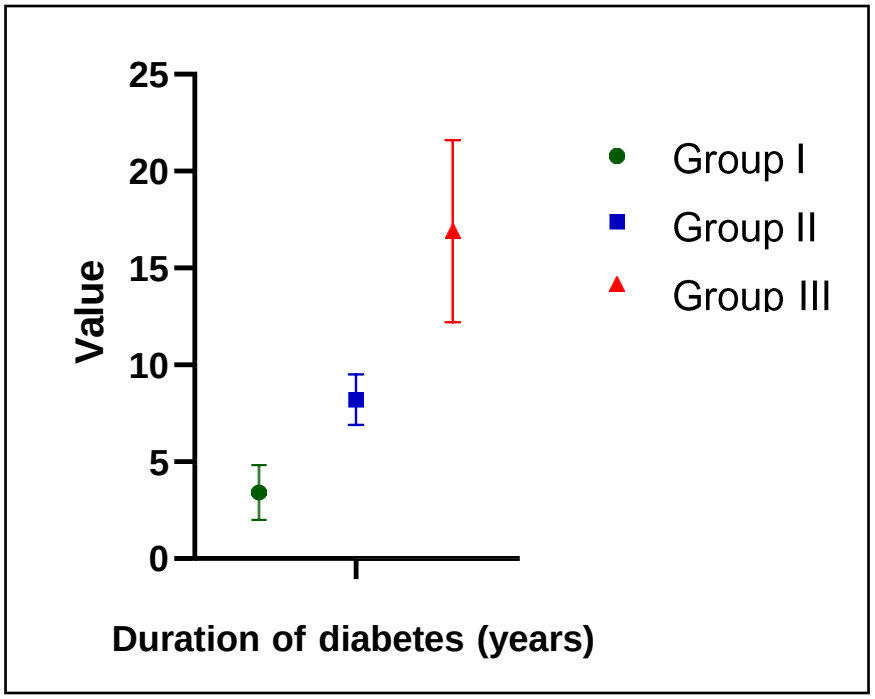
NS- Non-significant (p value: $p > 0.1$)

RESULTS

Table 2: Distribution of subjects as per their duration of diabetes.

Group	Duration of diabetes (Years)
Group I (N=50)	3.4 ± 1.4
Group II (N=50)	8.2 ± 1.3
Group III (N=50)	16.9 ± 4.7

Graph 1: Mean ± SD of the duration of diabetes in the respective group.

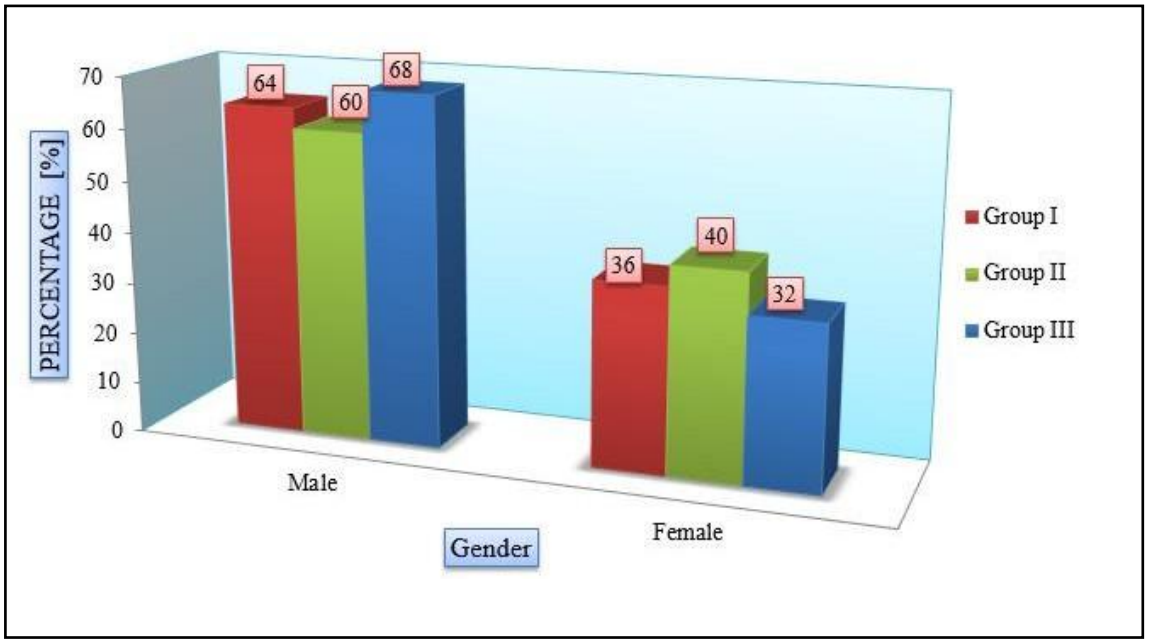


As we divided the study populations into three groups based on duration of diabetes, group I with diabetes duration of 1-5 years had mean duration of 3.4 ± 1.4 years. Group II with diabetes duration of 6-10 years had mean duration of 8.2 ± 1.3 years while group III with diabetes duration of more than 10 years had mean duration of 16.9 ± 4.7 years.

Table 3: Gender distribution of the subjects with respect to duration of diabetes.

Gender	Group I (N=50)		Group II (N=50)		Group III (N=50)	
	N	%	N	%	N	%
Male	32	64.0	30	60.0	34	68.0
Female	18	36.0	20	40.0	16	32.0
Total	50	100	50	100	50	100

Graph 2: Distribution graph of the gender in the respective group.

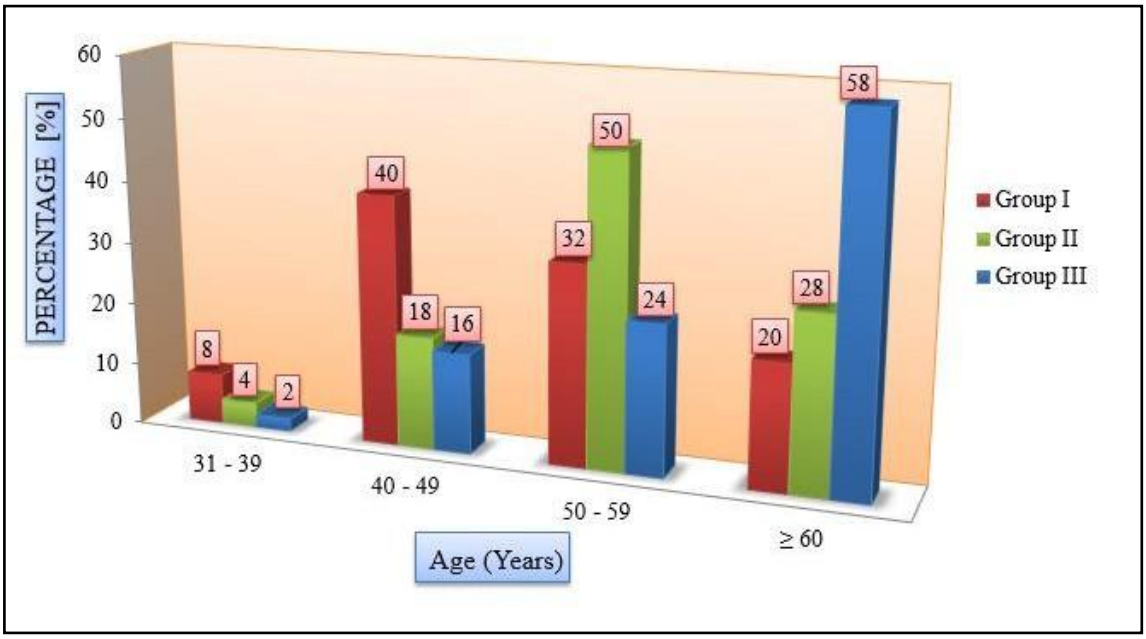


All three study groups were dominated by male gender. Group I had 64% males and 6% females while group II had 60% males and 40% females and group III had 68% males and 32% females.

Table 4: Age group distribution of the subjects with respect to duration of diabetes.

Age (Years)	Group I (N=50)		Group II (N=50)		Group III (N=50)	
	N	%	N	%	N	%
31 - 39	4	8.0	2	4.0	1	2.0
40 - 49	20	40.0	9	18.0	8	16.0
50 - 59	16	32.0	25	50.0	12	24.0
≥ 60	10	20.0	14	28.0	29	58.0
Total	50	100	50	100	50	100

Graph 3: Distribution graph of the age group in the respective group.



Coming to age group distribution, all the three groups were dominated by the patients with age more than 50 years. 32%, 50% and 24% in group I, group II and group III

respectively had age between 50-59 years while 20% in group I, 28% in group II and 28% in group III were geriatrics. Group I patients with diabetes duration of less than 5 years had larger subjects with age 31 – 49 years (48%) as compared to 22% in group II and 18% in group III.

Table 5: Mean ± SD of baseline characteristics with respect to duration of diabetes.

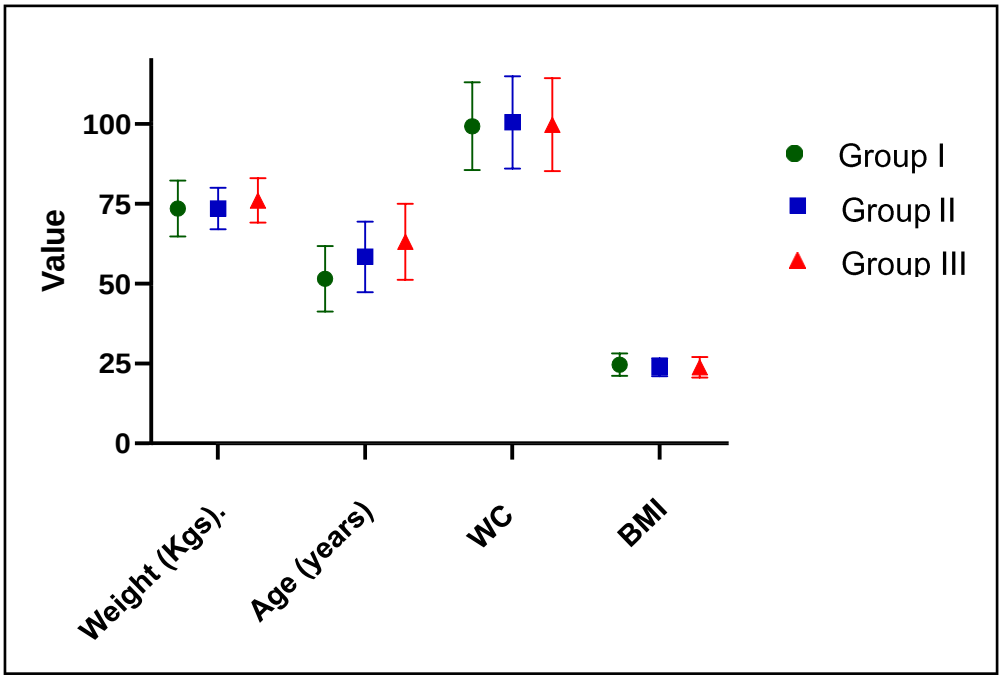
Variables	Group I (N=50)	Group II (N=50)	Group III (N=50)
Height (cm)	169.8 ± 14.4	172.1 ± 11.5	170.6 ± 12.3
Weight (Kgs)	73.5 ± 8.7	73.6 ± 6.5	76.1 ± 6.9
Age (years)	51.5 ± 10.2	58.4 ± 11.0	63.1 ± 11.9

The mean height of the subjects of group I, group II and group III was 169.8 ± 14.4 cm, 172.1 ± 11.5 cm and 170.6 ± 12.3 cm respectively. The mean weight was almost similar in all three groups with 73.5 ± 8.7 kg, 73.6 ± 6.5 Kg and 76.1 ± 6.9 Kg respectively. However, the mean age increased proportionately as the duration of diabetes increased as the mean age was 51.5 ± 10.2 years in group I which was lower as compared to 58.4 ± 11.0 years in group II and 63.1 ± 11.9 years in group III.

Table 6: Mean ± SD of anthropometric parameters with respect to duration of diabetes.

Anthropometric parameters	Group I (N=50)	Group II (N=50)	Group III (N=50)
WC	99.3 ± 13.8	100.5 ± 14.4	99.8 ± 14.6
WHR	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1
BMI	24.6 ± 3.5	23.8 ± 2.8	23.9 ± 3.2

Graph 4: Box plot of the anthropometric parameters in the respective group.

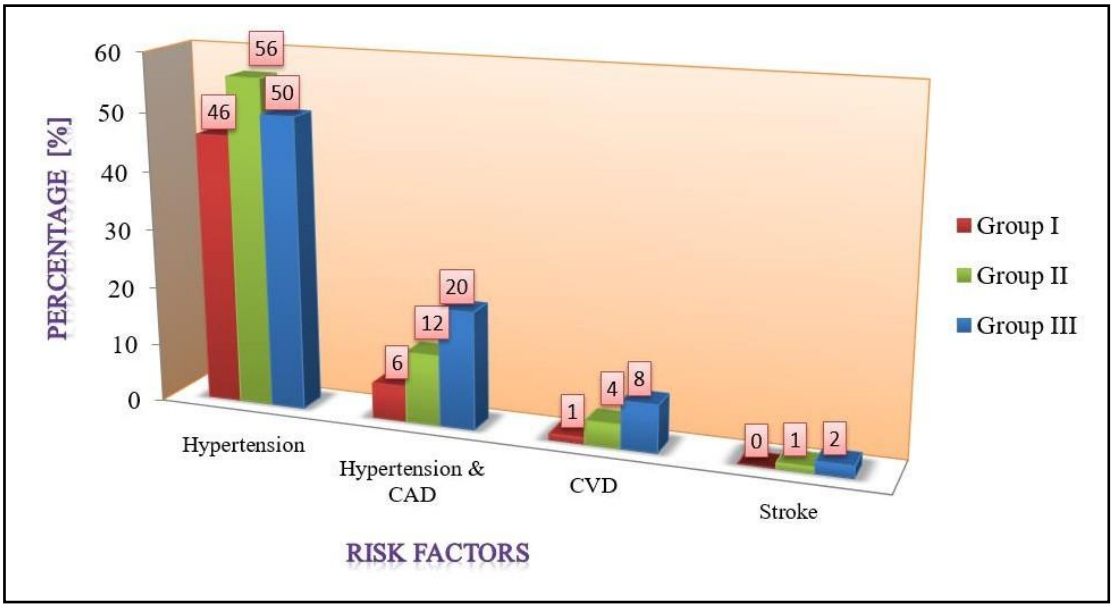


The mean waist circumference was 99.3 ± 13.8 cm, 100.5 ± 14.4 cm and 99.8 ± 14.6 in group I, group II and group III respectively. The mean BMI was 24.6 ± 3.5 kg/m^2 in group I, 23.8 ± 2.8 kg/m^2 in group II and 23.9 ± 3.2 kg/m^2 in group III.

Table 7: Presence of comorbidities in the respective study groups.

Comorbidities	Group I (N=50)	Group II (N=50)	Group III (N=50)
Hypertension	23 (46%)	28 (56%)	25 (50%)
Hypertension & CAD	3 (6%)	6 (12%)	10 (20%)
CVD	1 (1%)	2 (4%)	4 (8%)
Stroke	0	1 (1%)	1 (2%)

Graph 5: Distribution graphs of comorbidities in the respective study groups.

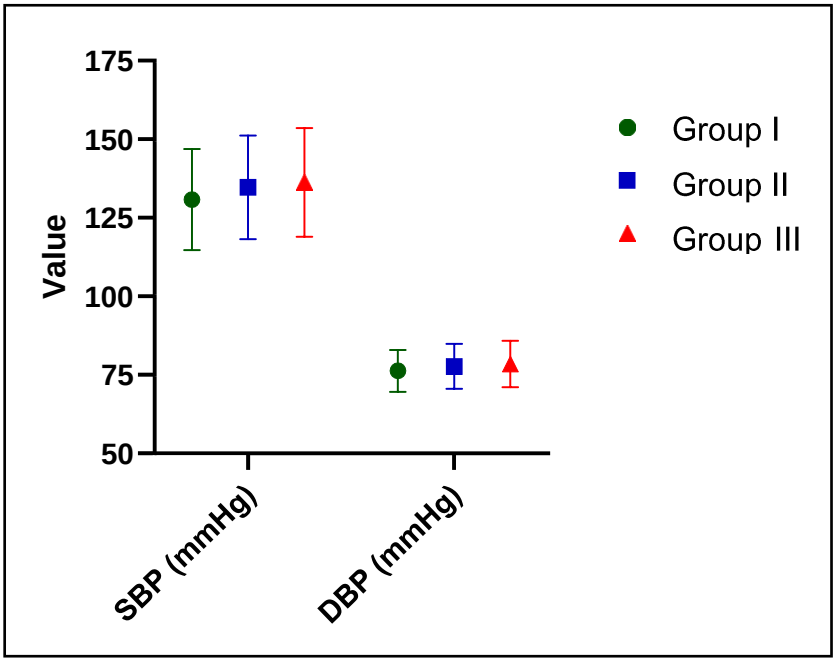


Alongside T2DM, majority of the patients had hypertension. For instance, 46% in group I, 56% in group II and 50% in group III had hypertension. While 6% in group I, 12% in group II and 20% in group III had hypertension and CAD. 8% in group III had CVD while one patient each in group II and group III had history of stroke.

Table 8: Mean ± SD of blood pressure parameters with respect to duration of diabetes.

Hemodynamic parameters	Group I (N=50)	Group II (N=50)	Group III (N=50)
SBP (mmHg)	130.8 ± 16.1	134.7 ± 16.5	136.3 ± 17.3
DBP (mmHg)	76.3 ± 6.7	77.7 ± 7.1	78.5 ± 7.4

Graph 6: Box plot of blood pressure parameters with respect to duration of diabetes.

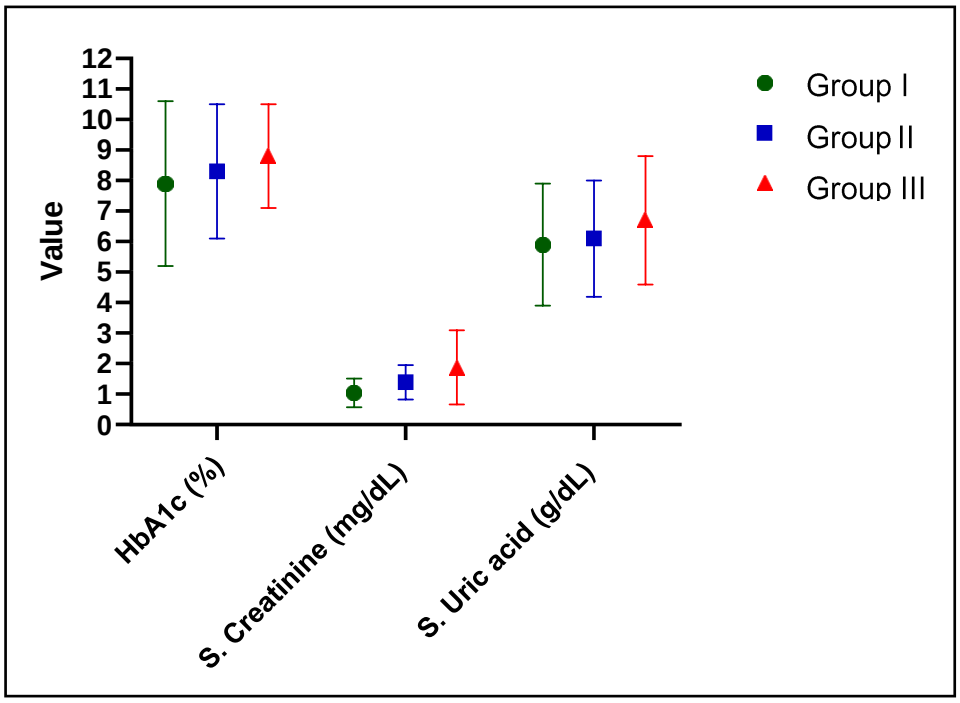


The mean systolic blood pressure (mmHg) was 130.8 ± 16.1, 134.7 ± 16.5 and 136.3 ± 17.3 in group I, group II and group III respectively. Similarly, the mean diastolic blood pressure (mmHg) was 76.3 ± 6.7, 77.7 ± 7.1, and 78.5 ± 7.4 in group I, group II and group III respectively.

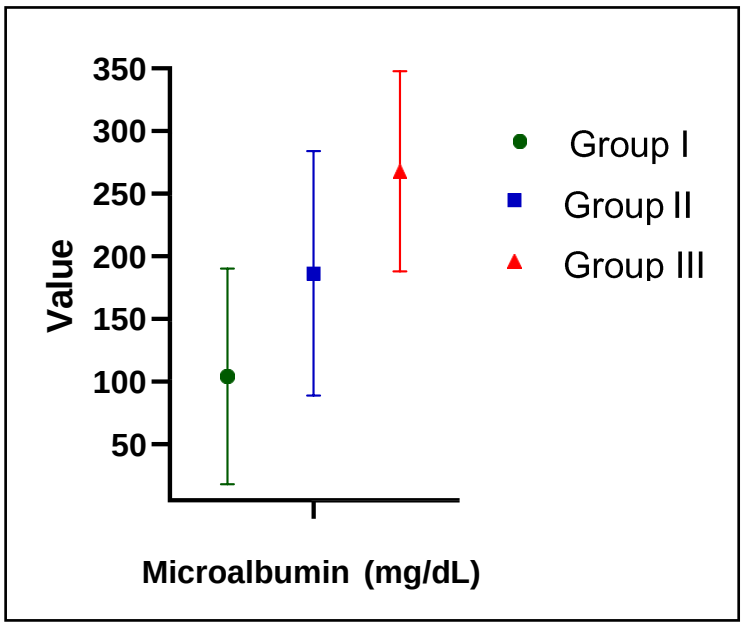
Table 9: Mean ± SD of laboratory parameters with respect to duration of diabetes.

Parameters	Group I (N=50)	Group II (N=50)	Group III (N=50)
HbA1c (%)	7.9 ± 2.7	8.3 ± 2.2	8.8 ± 1.7
Blood urea (mg/dL)	51.1 ± 40.2	52.0 ± 41.9	54.7 ± 43.9
S. Creatinine (mg/dL)	1.04 ± 0.47	1.19 ± 0.36	1.49 ± 1.03
S. Uric acid (g/dL)	5.9 ± 2.0	6.1 ± 1.9	6.7 ± 2.1
Microalbumin (mg/dL)	104.3 ± 86.1	186.4 ± 97.5	267.8 ± 79.9
ACR (mg/g creatinine)	198.0 ± 72.7	215.3 ± 68.1	259.7 ± 75.3
eGFR (mL/min/1.73 m^2)	78.8 ± 16.5	55.9 ± 12.7	46.5 ± 19.6

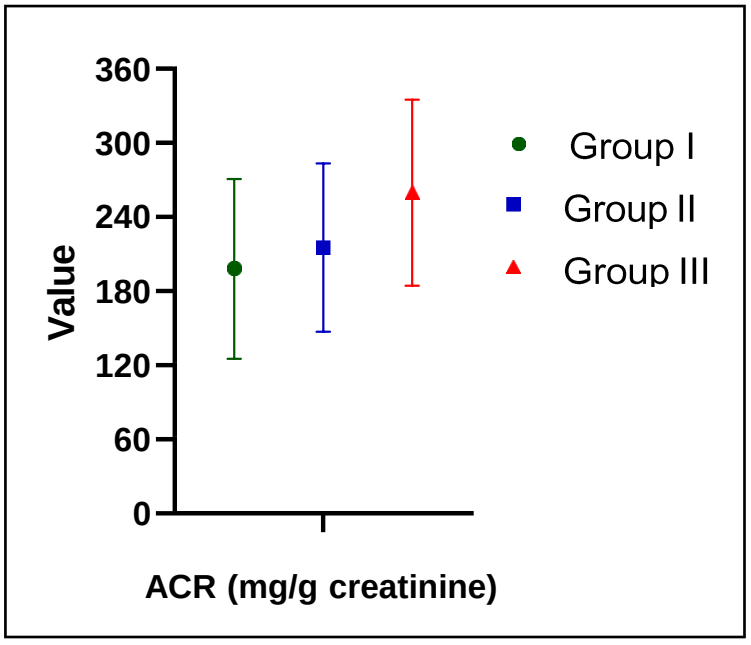
Graph 7: Box plot of laboratory parameters with respect to duration of diabetes.



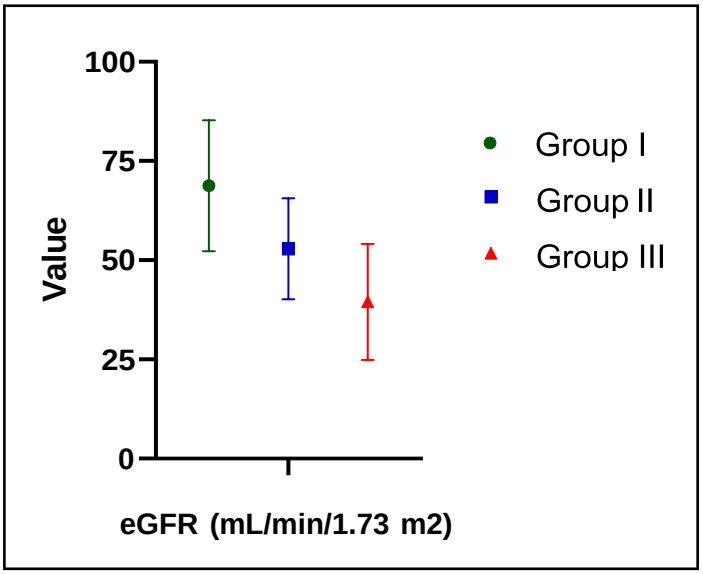
Graph 8: Box plot of microalbumin with respect to duration of diabetes.



Graph 9: Box plot of albumin-to-creatinine ratio with respect to duration of diabetes.



Graph 10: Box plot of eGFR with respect to duration of diabetes.

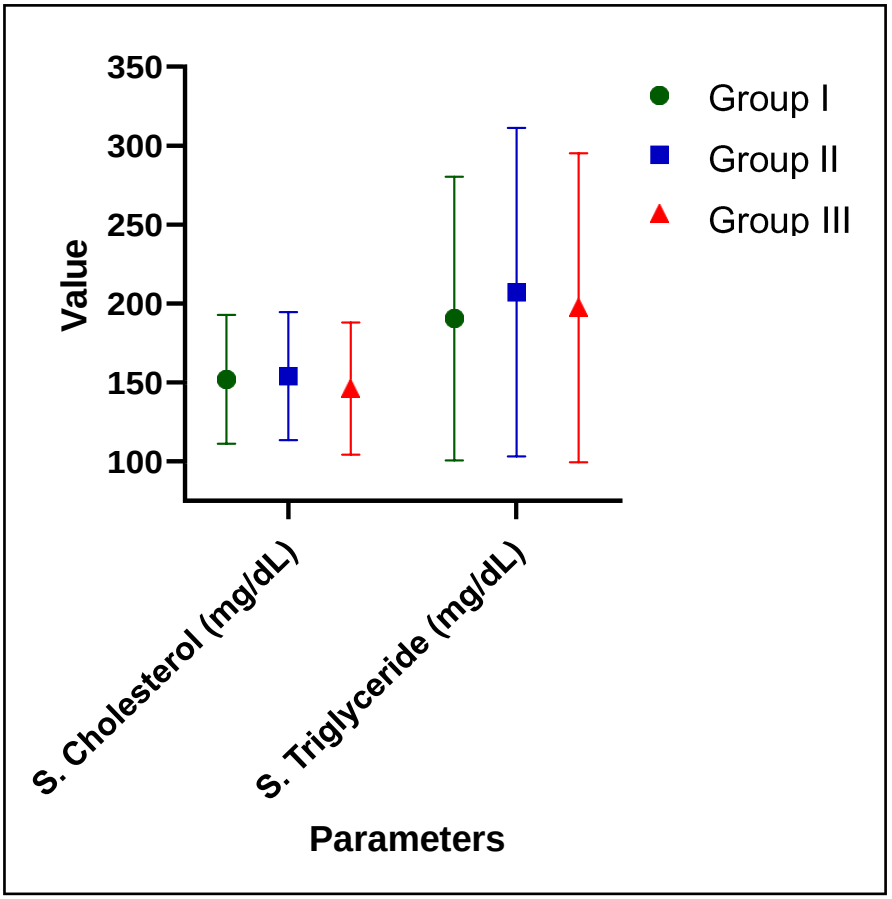


The above table depicts the lab parameters stratification in the respective categories of duration of diabetes. The mean ACR (mg/g creatinine) was 198.0 ± 72.7 in group I which was lower as compared to 215.3 ± 68.1 and 259.7 ± 75.3 in group II and group III respectively. The mean eGFR (mL/min/1.73 m^2) was 46.5 ± 19.6 in group III that was lower as compared to 55.9 ± 12.7 in group II and 78.8 ± 16.5 in group I. Coming to creatinine (mg/dL), group I had mean creatinine of 1.04 ± 0.47 while it was 1.19 ± 0.36 and 1.49 ± 1.03 in group II and group III respectively. The mean S. uric acid increased with increase in duration of diabetes with values of 5.9 ± 2.0, 6.1 ± 1.9 and 6.7 ± 2.1 in group I, group II and group III respectively. The mean HbA1c (%) in group I, group II and group III was 7.9 ± 2.7, 8.3 ± 2.2 and 8.8 ± 1.7 respectively while the mean microalbumin levels (mg/dL) were 104.3 ± 86.1, 186.4 ± 97.5 and 267.8 ± 79.9 respectively.

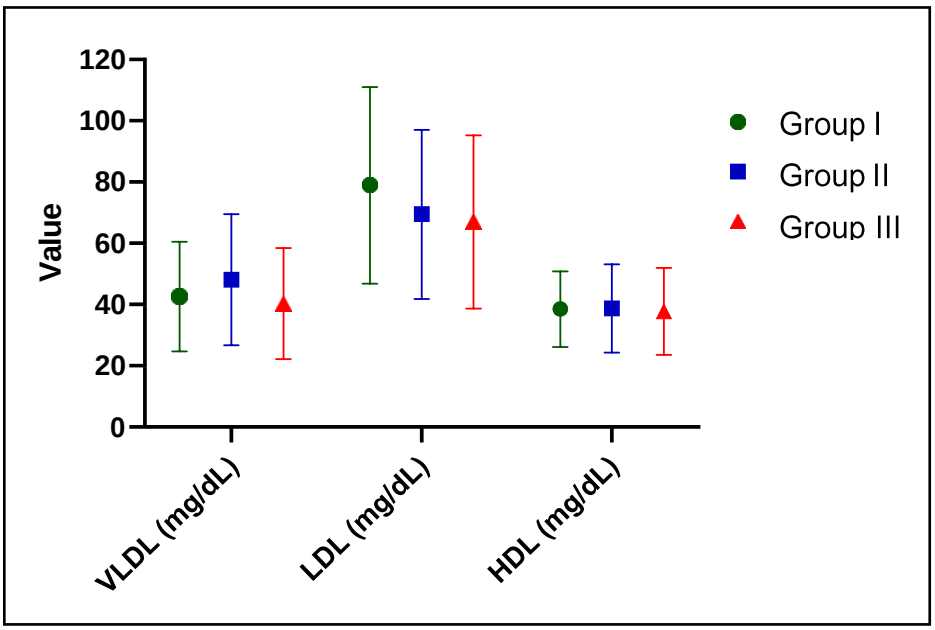
Table 10: Mean ± SD of lipid profile parameters with respect to duration of diabetes.

Lipid Profile	Group I (N=50)	Group II (N=50)	Group III (N=50)
S. Cholesterol (mg/dL)	151.9 ± 40.8	153.9 ± 40.5	146.1 ± 41.8
S. Triglyceride (mg/dL)	190.4 ± 89.9	207.1 ± 104.0	197.3 ± 97.9
VLDL (mg/dL)	42.6 ± 17.9	48.1 ± 21.4	40.3 ± 18.1
LDL (mg/dL)	79.0 ± 32.1	69.5 ± 27.6	66.9 ± 28.3
HDL (mg/dL)	38.5 ±12.4	38.8 ± 14.4	37.7 ± 14.2

Graph 11: Box plot of cholesterol & triglyceride with respect to duration of diabetes.



Graph 12: Box plot of lipid molecules with respect to duration of diabetes.

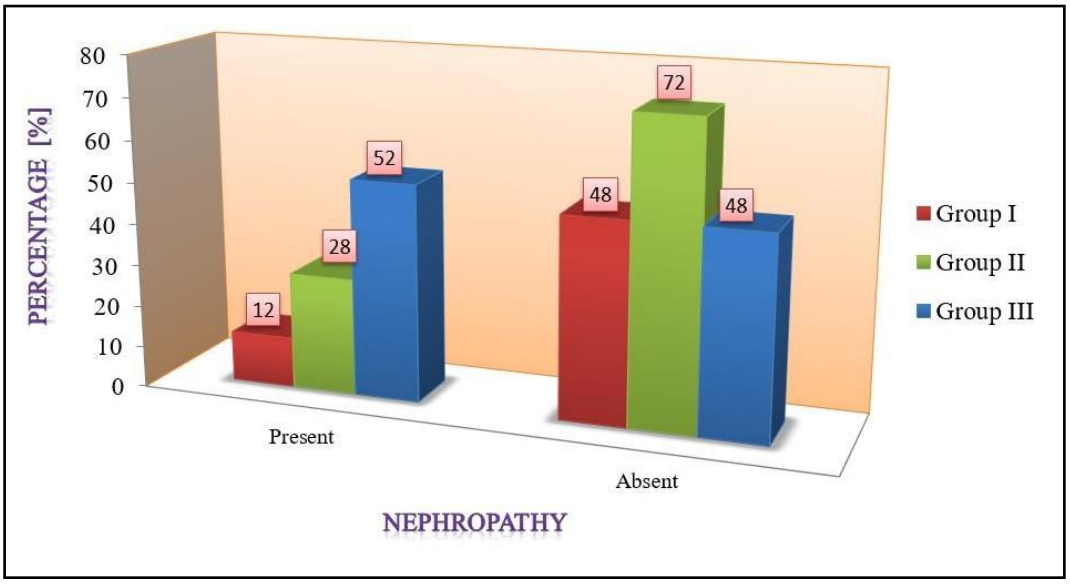


The S. Cholesterol level (mg/dL) was 151.9 ± 40.8, 153.9 ± 40.5 and 146.1 ± 41.8 in group I, group II and group III respectively while the mean S. Triglyceride (mg/dL) was 190.4 ± 89.9, 207.1 ± 104.0 and 197.3 ± 97.9 respectively. Coming to lipoprotein levels, the mean LDL (mg/dL) in group I, group II and group III was 79.0 ± 32.1, 69.5 ± 27.6 and 66.9 ± 28.3 respectively while mean HDL (mg/dL) was 38.5 ±12.4, 38.8 ± 14.4 and 37.7 ± 14.2 in group I, group II and group III respectively.

Table 11: Incidence of Nephropathy observed in the patients of each group.

Signs of Nephropathy	Group I (N=50)	Group II (N=50)	Group III (N=50)
Present	06 (12%)	14 (28%)	26 (52%)
Absent	44 (88%)	36 (72%)	24 (48%)
Significance: $\chi 2 = 19.06$; $P < 0.0001$.			

Graph 13: Distribution graph of Nephropathy observed in the patients of each group.



52% in the group III had diabetic nephropathy as compared to 28% and 12% in group II and group I respectively.

Table 12: Statistical analysis of patient parameters with respect to duration of diabetes.

Variable	Group I vs. Group II	Group I vs. Group III	Group II vs. Group III
Baseline variables			
Height (m)	t = 1.191 P = 0.2364	t = 0.383 P = 0.7022	t = -0.869 P = 0.3871
Weight (Kgs)	t = 0.0651 P = 0.9482	t = 1.656 P = 0.1010	t = 1.865 P = 0.0652
Age (years)	t = 3.252 P = 0.0016	t = 5.233 P < 0.0001	t = 2.051 P = 0.0430
Hemodynamic parameters			
SBP	t = 1.196 P = 0.234	t = 1.646 P = 0.1030	t = -0.473 P = 0.6371
DBP	t = 1.014 P = 0.3130	t = -1.558 P = 0.1224	t = -0.552 P = 0.5825

Anthropometric parameters			
WC	t = 0.425 P = 0.6715	t = 0.176 P = 0.8607	t = -0.241 P = 0.8098
BMI	t = -1.262 P = 0.2099	t = -1.044 P = 0.2992	t = 0.166 P = 0.8683
Lab parameters			
HbA1c	t = 0.812 P = 0.4187	t = 1.995 P = 0.0489	t = 1.272 P = 0.2065
Blood urea	t = 0.110 P = 0.9130	t = 0.428 P = 0.6698	t = 0.315 P = 0.7537
S. Creatinine	t = 3.385 P = 0.0010	t = -4.576 P < 0.0001	t = -2.599 P = 0.0108
S. Uric acid	t = 0.513 P = 0.6093	t = 1.951 P = 0.0540	t = 1.498 P = 0.1373
Microalbumin	t = 4.463 P < 0.0001	t = 9.843 P < 0.0001	t = 4.566 P < 0.0001
uACR	t = 1.228 P = 0.2224	t = 4.168 P = 0.0001	t = 3.092 P = 0.0026
eGFR	t = -5.40 P < 0.0001	t = -9.404 P < 0.0001	t = -4.897 P < 0.0001
Lipid profile			
S. Cholesterol	t = 0.246 P = 0.8062	t = -0.702 P = 0.4843	t = -0.948 P = 0.3451
S. Triglyceride	t = 0.859 P = 0.3924	t = 0.367 P = 0.7144	t = -0.485 P = 0.6286
VLDL	t = 1.394 P = 0.1665	t = -0.639 P = 0.5244	t = -1.968 P = 0.0519
LDL	t = -1.587 P = 0.1158	t = -1.999 P = 0.0483	t = -0.465 P = 0.6429
HDL	t = 0.112 P = 0.9113	t = -0.300 P = 0.7648	t = -0.385 P = 0.7014

Table 13: Multivariate linear regression analysis of all the variables w.r.t to uACR.

Variable	95% CI	|t|	P value
Intercept	-285.4 to 414.9	0.3658	0.7151
AGE (yrs)	-0.7894 to 1.468	0.5950	0.5529
SEX[F]	-41.80 to 7.129	1.402	0.1633
DURATION OF T2DM (YEARS)	-7.021 to -2.657	4.388	<0.0001
HEIGHT (cms)	-0.9349 to 1.628	0.5351	0.5935
WEIGHT (cms)	-1.945 to 1.063	0.5798	0.5631
WAIST CIRCUMFERENCE	-0.2214 to 1.584	1.493	0.1378
WAIST HIP RATIO	-22.45 to 245.4	1.647	0.1020
SBP	-0.3815 to 1.150	0.9928	0.3227
DBP	-2.810 to 0.5412	1.339	0.1828
Hb1AC	-5.570 to 11.92	0.7179	0.4741
eGFR	-0.7741 to -0.4733	8.204	<0.0001
S. CHOLESTROL	-0.6344 to 0.01403	1.893	0.0606
S.TRIGLYCERIDE	-0.1199 to 0.1420	0.1670	0.8676
VLDL	-0.9868 to 0.3003	1.055	0.2933
LDL	-0.3057 to 0.6563	0.7211	0.4722
HDL	-1.553 to 0.1063	1.725	0.0869
B. UREA	0.04872 to 0.5706	2.348	0.0204
S. CREATININE	-9.071 to 3.586	0.8575	0.0392

Table 14: Correlation of parameters with uACR.

Variable	r value	P value
eGFR	-0.714	0.0052
Duration of T2DM (years)	0.607	0.1001
S. Creatinine	-0.148	<0.001
Microalbumin	0.841	<0.0001

DISCUSSION

Given that more than 80% of the world's population lives in economically developing nations, it is very likely that the worldwide burden of illness due to diabetes mellitus will continue to escalate unless measures are taken to blunt the expected increase in the prevalence. Diabetic nephropathy is one of the major complications that develop over time in type 2 diabetes mellitus (T2DM). Commonly measured markers for the diagnosis and progression of DN include serum creatinine, eGFR, blood urea, and urinary albumin.[92] Early, detection of abnormal renal function is essential to slow down the progression to nephropathy stage and further to end-stage renal disease (ESRD). Despite the increased attention in various parts of the world on the role of the biochemical parameters in the disease progression and management of diabetes mellitus, there is still paucity of information on the interrelationship among these markers to one another and to presence of microvascular complications in Indian population in relation to the disease duration. Hence, the study was designed to determine the relationship between these biochemical parameters and disease duration (number of years with DM).

This was a cross-sectional observational study and 150 patients were recruited for the study. Fifty type 2 diabetic subjects were recruited each for three groups separated by disease durations, group I patients with duration of diabetes being 1-5 years, group II with duration of diabetes being 6-10 years and group III with duration of diabetes being >10 years. In the present study among 150 study subject's, male dominance was observed as 64% were males and the rest 36% were females. This was almost congruent to **Chowta et al.** study, where slightly more than half of the study subjects 59% were males and 41% females.[81] **Khadka et al.** reported that 52.8% were males and the remaining 47.2% were females while **Sana et al**. reported that 60.9% were males and 39.1% were females.[83,93] Coming to gender distribution in the present study with respect to duration of diabetes, 64% males and 36% females in group I, 60% were males and 40% were females in group II and in group III 68% males and 32% females were present. There was no significant difference in the gender distribution in all the three groups ($P>0.05$). **Buyyado et al.** reported that with respect to the duration of diabetes, in 0-4 years 61.2% were males and the rest 38.8% were females, in the group 5-9 years 62.2% were males and the rest 37.8% were females, in the group 10-14 years 61.5% were males and the rest 38.5% were females.[94] The mean age of the participants of the present study was in group I, II and III was 51.5 ± 10.2 years, 58.4 ± 11.0 years and 63.1 ± 11.9 years respectively. The patients with longer duration of diabetes group III were older when compared to the patients with

short duration of diabetes Group I. There was a significant difference in the age between the groups with respect to the duration of diabetes when group I vs group II was compared ($t = 3.252$, $P = 0.0016$); as well as strong significance in group I and group II ($t = 5.233$, $P < 0.0001$) while a borderline significance between group II and group III ($t = 2.051$, $P = 0.0430$). **Idowu et al.** reported that the mean age of the participants in newly diagnosed DM was 57.96 ±1.24 years. While the mean age of the participants in the patients with duration of diabetes 5-10 years and >10 years of the duration of diabetes was 62.64 ±1.22 years and 65.86 ±1.71 years respectively. With respect to age in our study, 4.6% of the study subjects were in third decade of life, 24.7 % were in fourth decade of life, 35.3% were in fifth decade of life and the remaining 35.3% were beyond sixth decade of the life.[80] **Karar et al**. reported that, 9% were between 30 and 50 years, 52% were between 51 and 70 years and 39% were above 70 years while **Khadka et al.** reported that 26.8% had age <50 years, 38.8% were in the age range of 50-59 years and 34.5% of the patients were geriatrics. Majority of the study were dominated by patients with age more than 50 years.[79,83]

Anthropometric measurements are noninvasive quantitative measurements of the body. Obesity has been identified as a risk factor for the development of diabetes and hypertension both linked with the development of DKD.[95] According to the World Health Organization (WHO), there are two separate classifications of obesity namely 'generalized', defined as body mass index (BMI, calculated as weight in kilograms (kg) divided by height in meters (m) squared) of ≥30 kg/m^2; and 'central/abdominal', assessed using waist circumference (WC) and/or waist-to-hip/height ratio (WHR/WHtR).[95] In the present study, the mean WC of the patients in group I, II and III was 99.3 ± 13.8 Cm, 100.5 ± 14.4 Cm and 99.8 ± 14.6 Cm respectively. There was no significant difference in the WC in between the three groups ($P>0.05$). Somewhat similar observations were reported by **Idowu et al.** in which WC in the patients with newly diagnosed DM was 94.62 ± 1.88 Cm, WC in patients with duration of diabetes 5-10 years was 94.82 ±1.98 Cm and WC was 98.10 ± 1.5 Cm in patients with duration of diabetes > 10 years.[80] **Kanakamani et al.** reported that the WC in the normoalbuminuric patients was 93.5 ± 9.1 Cm and in microalbuminuric patients was 95 ± 10.4 Cm.[96] **Hukportie DN et al.** reported that the median of the WC in the patients without diabetic nephropathy was 105.5 cm (96.5, 115) and in patients with DN was 106.7 (97.8, 116.8). The WHR in patients of the present study in all the three group was similar and it was found to be 1.0 ± 0.1. There was no significant difference in WHR between the three groups ($P>0.05$). **Hukportie DN et al.** reported that the median WHR in patients without DKD and with DKD was 0.62

(0.57, 0.68) and 0.63 (0.57,0.68) respectively.[88] **Blaslov K et al.** reported that the WHtR might be of a greater importance in association to CKD compared to other anthropometric parameters that indicate central obesity.[97] In the present study, there was no significant relationship between the WC and WHR and the presence of DKD and these observations are similar to the meta-analytical study by **Man REK et al**.[98]

In our study, the mean BMI of the patients in group II and group III was almost similar and it was found to be 23.8 ± 2.8 kg/m^2 and 23.9 ± 3.2 kg/m^2 respectively while the mean BMI in group I patients was slightly higher and it was found to be 24.6 ± 3.5 kg/m^2. However, there was no significant difference in BMI with respect to duration of diabetes (P>0.05). Similar to our observations, **Idowu et al**. also stated that the diabetics with longest disease duration of >10 years had least BMI (27.20 ± 0.71Kg/m2).[80] **Kanakamani et al.** reported that the mean BMI of normoalbuminuric patients was 26.3 ± 4.2 kg/m^2 and the mean BMI of macroalbuminuric patients was 26.9 ± 4.43 kg/m^2.[96] **Buyyado O et al.** the mean BMI in patients with duration of diabetes 0-4 years, 5-9 years, 10-14 years, 15-19 years and > 20 years was 32.6 ±5.4 Kg/m^2,32.4 ± 5.3 Kg/m^2, 32.2 ± 5.3 Kg/m^2, 31.8 ± 5.4 kg/m^2 and 31.6 ± 5.5 kg/m^2 respectively and they also didn't observe any significant difference between the groups.[94] Moreover, **Chowta et al.** reported that the mean BMI of microalbuminuric patients was 22.4 ± 6.9 kg/m2 and for normoalbuminuric patients it was 21.6 ± 4.2 kg/m2. The difference between the groups was not statistically significant.[81]

The mean SBP of the patients was 130.8 ± 16.1 mmHg, 134.7 ± 16.5 mmHg and

136.3 ± 17.3 mmHg of group I, group II and group III respectively while the mean DBP was 76.3 ± 6.7 mmHg, 77.7 ± 7.1 mmHg and 78.5 ± 7.4 mmHg respectively. The SBP and DBP values were not found to be significant difference (P>0.05). Similar to our observations with highest SBP being reported in patients of group III, **Idowu et al.** also showed that the diabetics with longest disease duration of >10 years had highest systolic BP (147.12±3.39mmHg).[80] **Efundem et al**. too concluded that microalbuminuria is associated with higher systolic and diastolic blood pressure.[82]

HbA1c is a measure for the mean level of blood glucose in the past 90 days.[99] The mean HbA1c (%) in group I, II and III was 7.9 ± 2.7, 8.3 ± 2.2 and 8.8 ± 1.7 respectively.

When mean HbA1c values were compared between group I and group II, there was no significant statistical difference between the groups (t=0.812, P=0.4187). Similarly, there exists no significant difference in mean HbA1c values group II and group III (t=1.272,

P=0.2605). But, there was a borderline significant difference (t = 1.995, P = 0.0489) in the mean HbA1c (%) value in group I (7.9 ± 2.7) and in group III (8.8 ± 1.7). **Verma et al.** reported that the mean HbA1c (%) in patients with duration of diabetes 0-1 years, 2-5 years and >5 years was 5.9 ± 2.2, 7.9 ± 3.0 and 12.8 ± 2.4 respectively and HbA1c levels showed a significant increase with the duration of diabetes however, their patients had duration of diabetes mostly less than 10 years.[100] **Idowu et al.** reported that the mean HbA1c in patients with newly diagnosed diabetes was 11.48 ± 0.67. While the mean HbA1c in patients with duration of diabetes 5-10 years and >10 years was 13.09 ± 0.74 and 10.48 ± 0.71 respectively.[80] **Khadka et al.** reported that the mean HbA1C in patients without and with microalbuminuria was 7.84 ± 1.93 and 8.48 ± 1.81 respectively.[83] **Varghese A et al.** reported that the mean HbA1c in normoalbuminuric patients was 9.1 ± 2.2 and the mean HbA1c in microalbuminuric patients was 11.5 ± 4.8.[90]

An increasing trend in the serum creatinine values was observed in our study as the duration of diabetes increased. There exists a significant difference in the serum creatinine values in group I (1.04 ± 0.47 mg/dL) and group III (1.49 ± 1.03 mg/dL) (t = 3.320, P=0.0013) as well as between group II and group III (t=2.642, P=0.0096). **Idowu et al**. reported that the serum creatinine in newly diagnosed DM was 97.27±5.09 umol/l, the serum creatinine in subjects with 5-10 years of duration of diabetes was 214.61±10.36 umol/l and in the serum creatinine in subjects with > 10 years of duration was 122.32±13.30 umol/l.[80] **Efundem et al.** stated that the mean serum creatinine concentration (p < 0.001) was higher in people with microalbuminuria (1.6 ± 0.1 mg/dL) as compared to those with normoalbuminuria (0.9 ± 0.03 mg/dL).[82]

The microalbumin level (mg/dL) in the present study was 267.8 ± 79.9 in group III followed by 186.4 ± 97.5 and 104.3 ± 86.1 in group II and I respectively. There was a significant difference when all the three groups were internally compared (P < 0.0001). Thus, we found microalbuminuria was more predominant in patients having duration of T2DM of more than 10 years and the similar observations were putforth by **Narang et al.** and **Dhonde et al.**[101,85]The urinary albumin-to-creatinine ratio (UACR) plays a significant role in predicting the future risk of diabetes mellitus.[102] The UACR was originally introduced into clinical practice to detect incipient DN, as reflected by urinary albumin excretion (UAE), but it has since been shown to be a marker that can predict a variety of important health outcomes, including cardiovascular events, kidney failure, and mortality.[103] In the present study, there was a positive correlation between the UACR and duration of diabetes. The mean uACR in group I patients was 198.0 ± 72.7 mg/g creatinine

and in group III patients, it was 259.7 ± 75.3 mg/g creatinine. There exists a greater significant difference in between the uACR in between group I and group III (t = 4.168, P = 0.0001) as well as between group II and group III (t = 3.092, P = 0.0026). We didn't observe any significant difference in ACR of patients with diabetes between 1–5 years and with 6-10 years (t = 1.228, P = 0.2224). **Sana MA et al**. also concluded that, UACR was higher in patients with uncontrolled T2DM (in terms of higher HbA1c value) and with a longer duration since diagnosis.[93] Contrast to our findings, **Idowu et al**. observed that the mean ACR in newly diagnosed patients was 23.61±2.12 and the ACR in the subjects with duration of diabetes 5-10 years was 30.56±5.59 and the mean ACR in the study subjects with duration of diabetes >10 years was 65.85±10.38.[80] **Khadka et al.** reported that the mean value of microalbumin/ urine creatinine ratio in patients without microalbuminuria was 19.47±5.0 and in patients with microalbuminuria was 119.41±84.08.[83]

The eGFR changes indicates the progression of CKD in patients with diabetes. In our study, there exist a significant statistical difference in the eGFR values in all the three groups (P<0.0001). A decreasing trend in the eGFR values was observed as the duration of diabetes increased. For instance, the eGFR (mL/min/1.73 m^2) was 78.8 ± 16.5 in group I which was higher as compared to 55.9 ± 12.7 in patients of group II which was again higher s compared to 46.5 ± 19.6 in patients of group III. **Buyadaa O et al.** also reported that the rates of eGFR decline were significantly greater in those with duration of diabetes > 20 years compared those with duration of diabetes < 5 years (− 1.82 vs − 1.52 mL/min/year; respectively).[94] **Decosmo et al.** showed that patients with lower GFR values, older age, and longer duration of diabetes have a 49% risk of developing eGFR <60 mL/min/1.73 m^2.[104] **Efundem et al.** reported the mean eGFR value was higher in patients with normoalbuminuria (101.3 ± 3.9 mL/min/1.7 m^2) when compared to the patients with microalbuminuria (46.5 ± 2.3 mL/min/1.7 m^2).[82] Microalbuminuria in adults who formed the majority of our study participants is believed to be an early risk marker for nephropathy. The overall incidence rate of diabetic nephropathy (DN) in the study was 30.7% with group III dominating with 52% incidence rate followed by 28% in group II and 12% in group I. Thus, higher the duration of diabetes, higher the incidences of nephropathy was observed ($\chi 2$ = 19.06; P < 0.0001). A study by **Kebede et al.** had reported DN 9.9% of the patients with duration of T2DM less than 6 years while 13.9% patients with duration of T2DM 6-10 years and 16.7% with T2DM more than 10 years had DN.[105] In the United Kingdom Prospective Diabetes Study, the prevalence rate of nephropathy in Types 2 diabetic patients was 30.8%, while in Mexican Americans was

31%.[106]

Multiple linear regression was carried out in order to find the association of uACR and other variables in which the duration of diabetes (P<0.0001), eGFR (P<0.0001), blood urea (P=0.0204) and creatinine (P=0.0392) were found to be significantly associated while cholesterol (P=0.060) and HDL levels (P=0.086) were borderline significant. Moreover, we also observed strong positive correlation between uACR and microalbumin levels (r=0.841; P<0.0001) and a weak correlation with creatinine (r=-0.148; P<0.001) but was found to be significant. We also observed strong negative correlation between eGFR and uACR (r=-0.741; P=0.0052) demonstrating the inverse relationship between the two parameters. **Dhonde et al.** also observed positive correlation between microalbuminuria and ACR which was statistically highly significant.[85] A study done by **Kiconco et al.** showed a weak association between microalbuminuria and estimated glomerular filtration rate (eGFR), but it was not statistically significant (eGFR), odds ratio = 1:2, and P = 0:824.[87] In a study done by **Kalima et al.**, decreased eGFR and microalbuminuria were noted as characteristic features of nephropathy. End-stage renal disease is characterized with irreversible renal damage.[107]

LIMITATIONS

Our study is also subject to limitations and one should consider following factors before generalizing our findings. First, the present study was cross sectional in design, thus longitudinal trends in the management of DKD and modifiable risk factors could not be under taken into account. Second, we did not collect certain important confounding variables such as: diet, anemia and drug history, which might impact on the results. However, ignored confounding factors are likely to cause false positive correlations rather than false negative results and that would be blessing in disguise taking the study design into consideration. The differences in our results and other comparative studies might be due to the study design, sample selection, and differences in population, genetic, race, duration of DM, age, sex, glycemic control, and other risk factors. The duration of DM in this study was determined from the year of diabetes diagnosis. Unfortunately, the exact time of onset of diabetes cannot be timed in most Type 2 DM patients since most patients seek health care later when symptoms of the disease become apparent. Thus, duration of DM in Type 2 diabetic patients should be interpreted with caution. The definition of albuminuria is another source of discrepancy, as well as the methods of measurement of albuminuria and urine collection which differs study to study. Therefore, we recommend a long-term cohort study addressing these limitations.

CONCLUSION

Fifty type 2 diabetic subjects were recruited each for three groups that were formed on the basis of disease durations i.e., group I patients with duration of diabetes being 1-5 years, group II with duration of diabetes being 6-10 years and group III with duration of diabetes being >10 years. All three groups were dominated by males. The patients with longer duration of diabetes group III were older when compared to the patients with short duration of diabetes Group I. There was no significant difference in the waist circumference, waist-to-hip ratio and BMI between the three groups ($P>0.05$). An increasing trend in the serum creatinine values was observed as the duration of diabetes increased. The mean urine ACR was higher in patients with longer duration of diabetes. Moreover, microalbuminuria was more predominant in patients having duration of T2DM of more than 10 years while a decreasing trend in the eGFR values was observed as the duration of diabetes increased. A strong positive correlation between uACR and microalbumin levels ($r=0.841$; $P<0.0001$) and a weak correlation with creatinine ($r=-0.148$; $P<0.001$) but was found to be significant. We also observed strong negative correlation between eGFR and urine ACR ($r=-0.741$; $P=0.0052$) demonstrating the inverse relationship between the two parameters. The overall incidence rate of diabetic nephropathy (DN) in the study was 30.7% with higher the duration of diabetes, higher the incidences of nephropathy. Routine screening for microalbuminuria in type 2 diabetic patients will certainly helpful for early detection of involvement of kidney and thus to minimize the burden of diabetic complications due to renal involvement. Also, screening for diabetic nephropathy must be performed at the time of diagnosis of diabetes mellitus, since such patient's may have had a silent form of DM for some time already.

REFERENCES

1. Sulaiman MK. Diabetic nephropathy; recent advances in pathophysiology and challenges in dietary management. Diabetol Metab Syndr. 2019; 11:7.
2. J.L. Gross, M.J. de Azevedo, S.P. Silveiro, L.H. Canani, M.L. Caramori, T. Zelmanovitz, Diabetic nephropathy: diagnosis, prevention, and treatment, Diabetes Care. 2005; 28:164–176.
3. Gheith O, Farouk N, Nampoory N, Halim MA, Al-Otaibi T. Diabetic kidney disease: worldwide difference of prevalence and risk factors. J Nephropharmacol. 2015;5(1):49-56.
4. L.A. Folan, K.R. Tuttle, Diabetic nephropathy: implications for renal and cardiovascular outcomes, Minerva Med. 2004;95:385–394.
5. Lièvre M, Marre M, Chatellier G, Plouin P, Réglier J, Richardson L, et al. The non-insulin-dependent diabetes, hypertension, microalbuminuria or proteinuria, cardiovascular events, and ramipril (DIABHYCAR) study: Design, organization, and patient recruitment. DIABHYCAR Study Group. Control Clin Trials. 2000; 21:383–96.
6. Abbate M, Zoja C, Remuzzi G. How does proteinuria cause progressive renal damage? J Am Soc Nephrol. 2006; 17:2974–84.
7. Tahrani A. A, Dubb K, Raymond N. T, Begum S, Altaf QA, Sadiqi H, et al. Cardiac autonomic neuropathy predicts renal function decline in patients with type 2 diabetes: a cohort study. Diabetologia. 2014;57(6):1249-56.
8. Parving HH, Mogensen C, Thomas M, Brenner B & Cooper M. Poor prognosis in proteinuric type 2 diabetic patients with retinopathy: insights from the RENAL study. QJM; 2005; 98(2):119-126.
9. Bakris GL, Molitch M. Microalbuminuria as a risk predictor in diabetes: the continuing saga. Diabetes Care. 2014; 37:867-875.
10. Mahajan K, Batra A. Obesity in adult asian indians- the ideal BMI cut-off. Indian Heart J. 2018;70(1):195.
11. Dabla PK. Renal function in diabetic nephropathy. World J Diabetes. 2010 ;1(2):48-56.
12. Retnakaran R, Cull CA, Thorne KI, Adler AI, Holman RR; UKPDS Study Group. Risk factors for renal dysfunction in type 2 diabetes: U.K. Prospective Diabetes Study 74. Diabetes 2006; 55: 1832–1839.

13. Paul Cockwell. Lori-Ann Fisher. The global burden of chronic kidney disease. The Lancet. 2020; 395 (10225):662-4.
14. Weil EJ, Lemley KV, Mason CC, et al. Podocyte detachment and reduced glomerular capillary endothelial fenestration promote kidney disease in type 2 diabetic nephropathy. Kidney Int. 2012;82(9):1010–1017.
15. Toyoda M, Najafian B, Kim Y, Caramori ML, Mauer M. Podocyte detachment and reduced glomerular capillary endothelial fenestration in human type 1 diabetic nephropathy. Diabetes. 2007;56(8):2155–2160.
16. Vithian K, Hurel S. Microvascular complications: pathophysiology and management. Clin Med (Lond). 2010;10(5):505-9.
17. Zelmanovitz T, Gerchman F, Balthazar AP, Thomazelli FC, Matos JD, Canani LH. Diabetic nephropathy. Diabetol Metab Syndr. 2009;1(1):10.
18. Ritz E, Orth SR. Nephropathy in patients with type 2 diabetes mellitus. N Engl J Med. 1999;341(15):1127-33.
19. Weil EJ, Lemley KV, Mason CC, Yee B, Jones LI, Blouch K, et al. Podocyte detachment and reduced glomerular capillary endothelial fenestration promote kidney disease in type 2 diabetic nephropathy. Kidney Int. 2012;82(9):1010-7.
20. Lim AKh. Diabetic nephropathy - complications and treatment. Int J Nephrol Renovasc Dis. 2014; 7:361-381.
21. Hypertension in Diabetes Study (HDS): I. Prevalence of hypertension in newly presenting type 2 diabetic patients and the association with risk factors for cardiovascular and diabetic complications. J Hypertens 1993; 11: 309-17.
22. Foggensteiner L, Mulroy S, Firth J. Management of diabetic nephropathy. J R Soc Med. 2001;94(5):210-7.
23. Grauer GF. Proteinuria: measurement and interpretation. Top Companion Anim Med. 2011;26(3):121-7.
24. Williams ME. Diabetic nephropathy: the proteinuria hypothesis. Am J Nephrol. 2005; 25(2):77-94.
25. Ezzidi I, Mtiraoui N, Kacem M, Chaieb M, Mahjoub T, Almawi WY. Identification of specific angiotensin-converting enzyme variants and haplotypes that confer risk and protection against type 2 diabetic nephropathy. Diabetes Metab Res Rev. 2009; 25:717–724.
26. Prasad P, Tiwari AK, Kumar KM, Ammini AC, Gupta A, Gupta R, et al. Chronic renal insufficiency among Asian Indians with type 2 diabetes: I. role of RAAS gene

polymorphisms. BMC Med Genet. 2006; 7:42–50.

27. Ballerman BJ, Zeidel ML, Gunning ME, Brenner BM. Vasoactive peptides and the kidney. In: Brenner BM, Rector FC, editors. The kidney. 4. Philadelphia: Saunders; 1991. pp. 510–583.
28. Yokoyama H, Okudaira M, Otani T, Sato A, Miura J, Takaike H et al. Higher incidence of diabetic nephropathy in type 2 than in type 1 diabetes in early-onset diabetes in Japan. Kidney Int. 2000;58: 302-11.
29. Allen KV, Walker JD. Microalbuminuria and mortality in long-duration type 1 diabetes. Diab Care. 2003; 26:2389–2391.
30. Wachtell K, Ibsen H, Olsen MH, Borch-Johnsen K, Lindholm LH, Mogensen CE, et al. Albuminuria and cardiovascular risk in hypertensive patients with left ventricular hypertrophy: the LIFE study. Ann Intern Med. 2003; 139:901–906.
31. Jerums G, MacIsaac RJ. Treatment of microalbuminuria in patients with type 2 diabetes mellitus. Treat Endocrinol. 2002;1(3):163-73.
32. Rossing P, Hommel E, Smidt UM, Parving HH. Reduction in albuminuria predicts a beneficial effect on diminishing the progression of human diabetic nephropathy during antihypertensive treatment. Diabetologia 1994; 37: 511-6
33. Apperloo AJ, de Zeeuw D, de Jong PE. Short-term antiproteinuric response to antihypertensive treatment predicts long-term GFR decline in patients with non-diabetic renal disease. Kidney Int 1994; 45 Suppl.: S174-8.
34. Mogensen CE, Keane WF, Bennett PH, et al. Prevention of diabetic renal disease with special reference to microalbuminuria. Lancet 1995; 346: 1080-4
35. Lovell HG. Angiotensin converting enzyme inhibitors in normotensive diabetic patients with microalbuminuria. Cochrane Database Syst Rev. 2001;(1):CD002183.
36. Bakris GL. Clinical importance of microalbuminuria in diabetes and hypertension. Curr Hypertens Rep. 2004;6(5):352-6.
37. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group: KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013; 3:1–150.
38. Dyer AR, Greenland P, Elliott P, Daviglus ML, Claeys G, et al. Evaluation of measures of urinary albumin excretion in epidemiologic studies. Am J Epidemiol. 2004; 160:1122–1131.
39. Jafar TH, Chaturvedi N, Hatcher J, Levey AS. Use of albumin creatinine ratio and urine albumin concentration as a screening test for albuminuria in an Indo-Asian

population. Nephrol Dial Transplant. 2007; 22 :2194–2200.

40. Brantsma AH, Atthobari J, Bakker SJ, Zeeuw D, Jong PE, Gansevoort RT. What predicts progression and regression of urinary albumin excretion in the nondiabetic population? J Am Soc Nephrol. 2007; 18:637–645.
41. Sanchez-Bayle M, Rodriguez-Cimadevilla C, Asensio C, Ruiz-Jarabo C, Baena J, Arnaiz P, Villa S, Cocho P. Urinary albumin excretion in Spanish children. Nino Jesus Group. Pediatr Nephrol. 1995; 9:428–430.
42. Singh A, Satchell SC. Microalbuminuria: causes and implications. Pediatr Nephrol. 2011 Nov;26(11):1957-65.
43. Rademacher ER, Sinaiko AR. Albuminuria in children. Curr Opin Nephrol Hypertens. 2009; 18:246–251.
44. Hanevold CD, Pollock JS, Harshfield GA. Racial differences in microalbumin excretion in healthy adolescents. Hypertension. 2008; 51 :334–338.
45. Cho H, Kim JH. Prevalence of microalbuminuria and its associated cardiometabolic risk factors in Korean youth: Data from the Korea National Health and Nutrition Examination Survey. PLoS One. 2017;12(6): e0178716.
46. Jarraya F, Lakhdar R, Kammoun K, Mahfoudh H, Drissa H, Kammoun S, et al. Microalbuminuria: a useful marker of cardiovascular disease. Iran J Kidney Dis. 2013 ;7(3):178-86.
47. Khosla N, Sarafidis PA, Bakris GL. Microalbuminuria. Clin Lab Med. 2006;26(3):635-53.
48. Kaufman DP, Basit H, Knohl SJ. Physiology, Glomerular Filtration Rate. [Updated 2022 Jul 18]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.
49. Deo A, Levey A.S. eGFR, Concept of. In: Vincent, JL., Hall, J.B. (eds) Encyclopedia of Intensive Care Medicine. Springer, Berlin, Heidelberg.2012.
50. Chronic Kidney Disease Prognosis Consortium, Matsushita K, van der Velde M, Astor BC, Woodward M, Levey AS, et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet. 2010;375(9731):2073-81.
51. Gaede P, Lund-Andersen H, Parving H, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. N Engl J Med. 2008;358(6):580–591.
52. Johnson C, Levey A, Coresh J, Levin A, Lau J, Eknoyan G. Clinical practice

guidelines for chronic kidney disease in adults: part I. definition, disease stages, evaluation, treatment, and risk factors. Am Fam Physician. 2004;70(5):869–985.

53. Yokoyama H, Kanno S, Takahashi S, Yamada D, Honjo J, Saito K, et al. M. Risks for glomerular filtration rate decline in association with progression of albuminuria in type 2 diabetes. Nephrol Dial Transplant. 2011;26(9):2924-30.
54. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al. Chronic Kidney Disease Epidemiology Collaboration. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med. 2006;145(4):247-54.
55. Ferreira JP, Girerd N, Pellicori P, Duarte K, Girerd S, Pfeffer MA, et al. Renal function estimation and Cockroft-Gault formulas for predicting cardiovascular mortality in population-based, cardiovascular risk, heart failure and post-myocardial infarction cohorts: The Heart 'OMics' in AGEing (HOMAGE) and the high-risk myocardial infarction database initiatives. BMC Med. 2016 Nov 10;14(1):181.
56. Smilde TD, van Veldhuisen DJ, Navis G, Voors AA, Hillege HL. Drawbacks and prognostic value of formulas estimating renal function in patients with chronic heart failure and systolic dysfunction. Circulation. 2006; 114:1572–80.
57. Michels WM, Grootendorst DC, Verduijn M, Elliott EG, Dekker FW, Krediet RT. Performance of the Cockcroft-Gault, MDRD, and new CKD-EPI formulas in relation to GFR, age, and body size. Clin J Am Soc Nephrol. 2010 Jun;5(6):1003-9.
58. Levey AS, Coresh J, Greene T, Marsh J, Stevens LA, Kusek J, et al. Expressing the MDRD study equation for estimating GFR with IDMS traceable (gold standard) serum creatinine values. J Am Soc Nephrol. 2005; 16:69.
59. Cirillo M, Anastasio P, De Santo NG: Relationship of gender, age, and body mass index to errors in predicted kidney function. Nephrol Dial Transplant. 2005; 20: 1791-1798.
60. Lin J, Knight EL, Hogan ML, Singh AK. A comparison of prediction equations for estimating glomerular filtration rate in adults without kidney disease. J Am Soc Nephrol. 2003; 14: 2573-2580.
61. Vervoort G, Willems HL, Wetzels JFM. Assessement of glomerular filtration rate in healthy subjects and normoalbuminuric diabetic patients: validity of a new (MDRD) prediction equation. Nephrol Dial Transplant. 2002; 17: 1909-1913.
62. Prakash Babaliche, Rishit A. Nadpara, Arif Maldar. Association Between Estimated Glomerular Filtration Rate and Microvascular Complications in Type II Diabetes

Mellitus Patients: A 1-Year Cross-Sectional Study. J.Natl. Med. Assoc. 2019; 111(1):83-87.

63. Rigalleau V, Lasseur C, Perlemoine C, Barthe N, Raffaitin C, Chauveau P, Combe C, Gin H. Cockcroft-Gault formula is biased by body weight in diabetic patients with renal impairment. Metabolism. 2006; 55:108–112.
64. Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function--measured and estimated glomerular filtration rate. N Engl J Med. 2006; 354:2473–2483.
65. Bloomgarden ZT. Diabetic nephropathy. Diabetes Care. 2008; 31:823–827.
66. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004; 351:1296–1305.
67. Inoue K, Streja E, Tsujimoto T, Kobayashi H. Urinary albumin-to-creatinine ratio within normal range and all-cause or cardiovascular mortality among U.S. adults enrolled in the NHANES during 1999-2015. Ann Epidemiol. 2021; 55:15-23.
68. Microvascular complications and foot care: standards of medical care in diabetes - 2020. American Diabetes Association. Diabetes Care. 2020; 43:0–51.
69. Gerstein HC, Mann JF, Yi Q, Zinman B, Dinneen SF, Hoogwerf B, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. JAMA.2001; 286:421–426.
70. Forman JP, Brenner BM: 'Hypertension' and 'microalbuminuria': the bell tolls for thee. Kidney Int.2006; 69:22–28.
71. Palaniappan L, Carnethon M, Fortmann SP: Association between microalbuminuria and the metabolic syndrome: NHANES III. Am J Hypertens.2003; 16:952–958.
72. Mykkänen L, Haffner SM, Kuusisto J, Pyorala K, Laakso M. Microalbuminuria precedes the development of NIDDM. Diabetes.1994; 43:552–557.
73. Brantsma AH, Bakker SJ, Hillege HL, de Zeeuw D, de Jong PE, Gansevoort RT, PREVEND Study Group. Urinary albumin excretion and its relation with C-reactive protein and the metabolic syndrome in the prediction of type 2 diabetes. Diabetes Care. 2005; 28:2525–2530.
74. Christian A. H., Mochari H., Mosca L. J. Waist circumference, body mass index, and their association with cardiometabolic and global risk. Journal of the Cardio Metabolic Syndrome. 2009;4(1):12–19.
75. Misra A, Chowbey P, Makkar BM, Vikram NK, Wasir JS, Chadha D, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for

Asian Indians and recommendations for physical activity, medical and surgical management. J Assoc Physicians India 2009; 57:163-70.

76. Kodama S, Horikawa C, Fujihara K, Heianza Y, Hirasawa R, Yachi Y, et al. Comparisons of the strength of associations with future type 2 diabetes risk among anthropometric obesity indicators, including waist-to-height ratio: a meta-analysis. Am J Epidemiol. 2012;176(11):959–969.
77. Ruster C & Wolf G. Adipokines promote chronic kidney disease. Nephrol Dial Transplant.2013;28:8–14.
78. Ferreira ES, da Silva LS, da Costa GD, Moreira TR, Borges LD, Cotta RMM. Dietary intake, anthropometric measurements, biochemistry profile and their associations with chronic kidney disease and diabetes mellitus. J Nutr Sci. 2020; 9:e45.
79. Karar T, Alniwaider RR, Fattah MA, Al Tamimi W, Alanazi A, Qureshi S. Assessment of microalbuminuria and albumin creatinine ratio in patients with type 2 diabetes mellitus. J Nat Sc Biol Med.2015; 6: S89-92.
80. Idowu AA, Ajose AO, Adedeji AT, Adegoke AO, Jimoh KA. Microalbuminuria, Other Markers of Nephropathy and Biochemical Derangementsin Type 2 Diabetes Mellitus: Relationships and Determinants. Ghana Med J. 2017;51(2):56-63.
81. Chowta NK, Pant P, Chowta MN. Microalbuminuria in diabetes mellitus: Association with age, sex, weight, and creatinine clearance. Indian J Nephrol. 2009;19(2):53-56.
82. Efundem NT, Assob JCN, Feteh VF, Choukem SP. Prevalence and associations of microalbuminuria in proteinuria-negative patients with type 2 diabetes in two regional hospitals in Cameroon: a cross-sectional study. BMC Res Notes. 2017;10(1):477.
83. Khadka B, Tiwari ML, Timalsina B, Risal P, Gupta S, Acharya D. Prevalence and Factors Associated with Microalbuminuria among Type 2 Diabetic Patients: A Hospital Based Study. JNMA J Nepal Med Assoc. 2018;56(209):516-521.
84. Muddu M, Mutebi E, Ssinabulya I, Kizito S, Mulindwa F, Kiiza CM. Utility of albumin to creatinine ratio in screening for microalbuminuria among newly diagnosed diabetic patients in Uganda: a cross sectional study. Afr Health Sci. 2019;19(1):1607-1616.
85. Dhonde S, Jagtap PE, Belwalkar GJ, Mane V, Shilwant N, Nagane NS. A study of microalbuminuria in patients with type 2 diabetes mellitus, visiting tertiary care center Sangli. Int J Clin Biochem Res 2022; 9(1):31-37.
86. Jatoi N, Said A H, Al-Ghamdi M S, M F. Al-Abdulmhsin, R A. Bin-Jaban, J A. Al-Tayeb, et al. Prevalence of Microalbuminuria and Cardiovascular Risk Factors in Patients With Diabetes Mellitus Type-II in Al-Khobar, Kingdom of Saudi Arabia.

Cureus. 2022;14(10): e29808.

87. Kiconco R, Rugera SP, Kiwanuka GN. Microalbuminuria and Traditional Serum Biomarkers of Nephropathy among Diabetic Patients at Mbarara Regional Referral Hospital in South Western Uganda. J Diabetes Res. 2019; 2019:3534260
88. Hukportie DN, Li FR, Zhou R, Zheng JZ, Wu XX, Wu XB. Anthropometric Measures and Incident Diabetic Nephropathy in Participants with Type 2 Diabetes Mellitus. Front Endocrinol (Lausanne). 2021; 12:706845.
89. Atre S, Deshmukh S, Kulkarni M, Prevalence of type 2 diabetes mellitus (T2DM) in India: A systematic review (1994–2018), Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(5):897-906.
90. Varghese A, Deepa R, Rema M, Mohan V. Prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetes centre in southern India. Postgrad Med J. 2001 Jun;77(908):399-402.
91. Kelsey JL, Whittemore AS, Evans AS, Thompson WD. Methods in Observational Epidemiology. Oxford University Press, 1996.
92. Campion CG, Sanchez-Ferras O, Batchu SN. Potential Role of Serum and Urinary Biomarkers in Diagnosis and Prognosis of Diabetic Nephropathy. Can J Kidney Health Dis. 2017; 4:2054358117705371.
93. Sana MA, Chaudhry M, Malik A, Iqbal N, Zakiuddin A, Abdullah M. Prevalence of Microalbuminuria in Type 2 Diabetes Mellitus. Cureus. 2020;12(12):e12318.
94. Buyadaa O, Salim A, Morton JI, Magliano DJ, Shaw JE. Rate of decline in kidney function and known age-of-onset or duration of type 2 diabetes. Sci Rep. 2021;11(1):14705.
95. World Health Organisation Overweight and Obesity Fact Sheet. [Accessed on 20 Oct, 2022)]. Available online: http://www.who.int/mediacentre/factsheets/fs311/en/.
96. Kanakamani, J, Ammini, A.C, Gupta, Nandita, Dwivedi, S.N. Prevalence of Microalbuminuria Among Patients with Type 2 Diabetes Mellitus—A Hospital-Based Study from North India. Diabetes Technology & Therapeutics. 2010; 12(2), 161–166.
97. Blaslov K, Bulum T, Duvnjak L. Waist-to-height ratio is independently associated with chronic kidney disease in overweight type 2 diabetic patients. Endocr Res. 2015;40(4):194-8.
98. Man REK, Gan ATL, Fenwick EK, Gupta P, Wong MYZ, Wong TY, et al. The Relationship between Generalized and Abdominal Obesity with Diabetic Kidney Disease in Type 2 Diabetes: A Multiethnic Asian Study and Meta-Analysis. Nutrients. 2018;10(11):1685.

99. Pecoits-Filho R, Abensur H, Betônico CC, Machado AD, Parente EB, Queiroz M, et al. Interactions between kidney disease and diabetes: dangerous liaisons. Diabetol Metab Syndr. 2016; 8:50.
100. Verma M, Paneri S, Badi P, Raman PG. Effect of increasing duration of diabetes mellitus type 2 on glycated hemoglobin and insulin sensitivity. Indian J Clin Biochem. 2006;21(1):142-6.
101. Narang U, Jagadhami V, Singla M, Singal K, Agarwal R, Arora M. A Study of Prevalence of Microalbuminuria and Diabetic Retinopathy in Rural Patients Presenting to a Tertiary Care Hospital in North India. International Journal of Contemporary Medical Research 2019; 6(8):18-22
102. Newman D.J, Pugia M.J, Lott J.A, Wallace J.F, Hiar A.M. Urinary protein and albumin excretion corrected by creatinine and specific gravity. Clin. Chim. Acta. 2000; 294:139–155.
103. Hayashi Y. Detection of Lower Albuminuria Levels and Early Development of Diabetic Kidney Disease Using an Artificial Intelligence-Based Rule Extraction Approach. Diagnostics (Basel). 2019;9(4):133.
104. De Cosmo S, Viazzi F, Pacilli A, Giorda C, Ceriello A, Gentile S, et al. Predictors of chronic kidney disease in type 2 diabetes: A longitudinal study from the AMD Annals initiative. Medicine (Baltimore). 2016;95(27):e4007.
105. Kebede SA, Tusa BS, Weldesenbet AB, Tessema ZT, Ayele TA. Incidence of Diabetic Nephropathy and Its Predictors among Type 2 Diabetes Mellitus Patients at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. J Nutr Metab. 2021; 21:6757916.
106. Adler AI, Stevens RJ, Manley SE, Bilous RW, Cull CA, Holman RR UKPDS GROUP. Development and progression of nephropathy in type 2 diabetes: The United Kingdom Prospective Diabetes Study (UKPDS 64) Kidney Int. 2003; 63:225–32.
107. Kalima N, Gabriel B. K, Muhindo R, Muyingo A. Chronic kidney disease in patients admitted to the medical ward of Mbarara Regional Referral Hospital in southwestern Uganda: prevalence and associated factors. Int.j.med.biomed.res 2015;4(2):107–116.

ANNEXURE - I

CLINICAL PROFORMA

Particulars of the patient:

1. Name:
2. Age:
3. Sex:
4. Occupation:
5. D.O.A
6. D.O.D

History:

Presenting complaints (with duration, onset, associated factors)

1. Polyuria
2. Polyphagia
3. Polydipsia
4. Weight loss/gain
5. Nocturnal diarrhea/constipation
6. Hypoglycemic unawareness
7. Bladder/bowel incontinence
8. Impotence
9. Postural dizziness
10. History of significant cardiovascular / cerebrovascular disease / thyroid disorder.

Past History: History of Tuberculosis, Diabetes, CAD, COPD, Asthma, Seizures.

Family history: Special consideration to HTN, DM, TB, CAD, CVA

Personal History:

1. Dietary-
2. Sleep-
3. Bladder and bowel-
4. Smoking-
5. Alcohol-
6. Treatment History:

General Physical examination:

1. Built
2. Nutrition
3. Height(cm)/Weight(cm)/Waist(cm)
4. Waist Hip ratio:
5. BMI
6. Pallor/Icterus/Clubbing/Cyanosis/Lymphadenopathy/Oedema
7. Vitals: BP
8. Pulse
9. Respiratory Rate
10. JVP

Investigations:

1. Fasting Blood glucose
2. Post Prandial Blood Glucose
3. Blood Urea
4. Serum Creatinine
5. Urine routine, microscopic analysis and microalbumin
6. Lipid profile
7. HbA1c

ANNEXURE - II

CONSENT FORM

SANTOSH MEDICAL COLLEGE AND HOSPITAL, GHAZIABAD, UP

I_____S/o/D/o/W/o_____R/o_____have been explained about the risks of this study by Dr. Nimish Kumar. I volunteer to take part in the study titled **"Study of Microalbuminuria and Albumin - Creatinine Ratio in Type 2 Diabetes Mellitus and Their Correlation With GFR, Anthropometry and Other Biochemical Parameters"** and have also been explained the purpose of this study to my satisfaction. I have been informed that in case of any adverse reaction, the treatment and compensation will be theresponsibility of the investigator.

My details will be kept confidential and I have the freedom to withdraw from the study at any point of time. I have been explained that I am under no risk while participating in this study.

I hereby give my consent to be enrolled in this study.

Signature of volunteer/guardian Signature of investigator

Telephone number

Signature of witness Date:

संतोष मेडिकल कॉलेज एवं अस्पताल (गाजियाबाद)

सहमति पत्र (सूचित)

मैं _____ बेटा / बेटी /पत्नी_____

निवासी _____ घोषणा करती हूं कि मैं डॉ._____, ने मुझे मेरी भाषा में अपने अध्ययन **"Study of Microalbuminuria and Albumin - Creatinine Ratio in Type 2 Diabetes Mellitus and Their Correlation With GFR, Anthropometry and Other Biochemical Parameters"** अध्ययन के उद्देश्य के बारे में , और अध्ययन के दौरान अपनाई जाने वाली विभिन्न प्रयोगशाला जांच के बारे में सूचित कर दिया है। मुझे अध्ययन की अवधि और उसके दौरान अपनाए जाने वाले निर्देश भी मेरी भाषा मे समझा दिए गए है| मैं उपरोक्त अध्ययन में बिना किसी दबाव के दाखिला ले रहा हूं और पूर्ण सहमति दे रहा हूं | सन्तोष अस्पताल, गाजियाबाद में अपने आगे के उपचार पर बिना प्रतिकूल प्रभाव डाले इस अध्ययन से और प्रयोगशाला जांच की प्रकृति से मैं जब चाहूँ बाहर जाने के अपने अधिकार को सुरक्षित रख रही हूं|

रोगी / रोगी के रिश्तेदार के हस्ताक्षर डॉक्टर के हस्ताक्षर

नाम

दिनांक:

मेरी उपस्थिति में मरीज ने पूरी तरह से डॉक्टर के बताए गए अध्ययन और निर्देशों को समझने के बाद अपनी स्वतंत्र इच्छा से ऊपर के फार्म पर हस्ताक्षर किए है।

हस्ताक्षर नाम:

पद नाम: पीजी

आयुर्विज्ञान चिकित्सा विभाग

ANNEXURE - III

PATIENT INFORMATION SHEET

1. OPD no:
2. Name:
3. Age:
4. Sex:
5. Address:
6. Phone number:

We invite you / your patient to participate in the research study titled study of being conducted in Santosh Medical College and Hospitals, Ghaziabad.

In accordance with the rules of ethical committee, a written consent will be taken. The relevant history will be asked and clinical examination of the patient will be done. Only the results of the investigations that you / your patient has already underwent as standard of care for such condition, are required for the study and no additional investigation will be done for the study. Special investigations, if any, was sent as per the discretion of the treating physician and no additional investigation was conducted for the purpose of the study. You / your patient identity will be kept confidential throughout the study and thereafter. You are free to withdraw from the study any time without any loss of rights to undergo treatment in this hospital.

For any further questions regarding the study, you can contact the investigator of study atthe following number: Dr. Nimish Kumar [+91 7709399434].

ANNEXURE – IV

ETHICAL & SCIENTIFIC BOARD COMMITTEE CERTIFICATE

SANTOSH
Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

F. No. SU/2021/1830[20] Dated: 17.07.2021

Subject: Grant of Ethical Clearance for Thesis Protocol Topic "**STUDY OF MICROALBUMINURIA , ACR IN TYPE 2 DM AND THEIR CORRELATION WITH GFR, ANTHROPOMETRY AND OTHER BIOCHEMICAL PARAMTERES.",** submitted by **Dr. Nimish Kumar,** MD/MS student of Batch 2020-2021, Department of **General Medicine**.

*****

With reference to his/her request for grant of Ethical Clearance for the Thesis Protocol entitled **"STUDY OF MICROALBUMINURIA , ACR IN TYPE 2 DM AND THEIR CORRELATION WITH GFR, ANTHROPOMETRY AND OTHER BIOCHEMICAL PARAMTERES.", Dr. Nimish Kumar** is informed that the Thesis Protocol submitted by him/her was considered by the **Screening Committee** of the Santosh Medical College & Hospital in its meetings held on 19.03.2021, 22.03.2021, 24.03.2021, 25.03.2021, 26.03.2021, 27.03.2021 and 06.04.2021. The recommendations of the **Screening Committee** were considered in detail by the Institutional **Ethics Committee** in its meeting held on **12.07.2021** and the same was **approved** by the **Ethics Committee**.

He /She is informed accordingly for further necessary action.

[Dr. V. P. Gupta]
REGISTRAR

SANTOSH DEEMED TO BE UNIVERSITY REGISTRAR GHAZIABAD, NCR DELHI

Dr. Nimish Kumar
MD/MS student of batch 2020-2021
Department of General Medicine
Email: nimish344@gmail.com

Copy to:

1. The Vice Chancellor
2. The Dean, SMC&H
3. The Dean – Research
4. The Dean – Academics
5. The Director - IQAC
6. Dr Ashok kumar (Guide)
7. HOD of **General Medicine**

Ouriginal
by Turnitin

Document Information

Analyzed document	nimish thesis intro , rol , discussion.docx (D150382138)
Submitted	11/21/2022 11:26:00 AM
Submitted by	Dr Jyoti Batra
Submitter email	drjyotibatra89@gmail.com
Similarity	8%
Analysis address	drjyotibatra89.sug@analysis.urkund.com

Sources included in the report

W	URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4630772/ Fetched: 1/2/2020 12:21:39 PM	5
W	URL: https://www.semanticscholar.org/paper/Assessment-of-microalbuminuria-and-albumin-ratio-in-Kara... Fetched: 11/21/2022 11:40:59 AM	1
W	URL: https://bmcresnotes.biomedcentral.com/articles/10.1186/s13104-017-2804-5 Fetched: 10/22/2019 12:07:25 PM	4
W	URL: https://www.researchgate.net/publication/11650509_Diabetic_nephropathy_Prevention_and_treatment Fetched: 5/17/2021 11:23:51 AM	1
W	URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4206379/ Fetched: 10/2/2019 3:13:39 PM	5
W	URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4048496/ Fetched: 5/6/2020 6:51:26 AM	1
W	URL: https://pubmed.ncbi.nlm.nih.gov/30058635/ Fetched: 1/14/2022 11:21:07 AM	1
W	URL: https://www.hindawi.com/journals/jdr/2019/3534260/ Fetched	2

Sr.No	Baseline characteristics			DURATION OF T2DM	Anthropometric parameters				Blood Pressure		ACE INHIBITORS	HbIAC (%)	ACR (mg/g creatinine)	Lipid Profile					Lab parameters		
	AGE (Years)	SEX	COMORBIDITIES	(Years)	HEIGHT (cms)	WEIGHT (cms)	WAIST CIRCUMFERENCE	WAIST HIP RATIO	SBP	DBP				% CHOLESTROL (mg/dL)	%TRIGLYCERIDE (mg/dL)	VLDL (mg/dL)	LDL (mg/dL)	HDL (mg/dL)	B. UREA (mg/dL)	CREATININE (mg/dL)	eGFR (mL/min/1.73 m2)
1	45	M	T2DM	3	186	72	81.2	0.98	120	70	NO	12.72	139.9	210	150	52	83	26	19	1.4	68
2	55	M	T2DM, HTN	2	175	69	76.4	0.97	140	70	YES	11.6	240	193	127	50	145	42	29	1.2	56.2
3	56	M	T2DM,CAD	4	178	65	82.9	1	130	70	NO	8.05	200	105	60	12	42	52	51	1.5	59.7
4	52	F	T2DM,HTN	4	170	85	98.3	1.01	140	80	YES	7.57	94	170	151	49	72	28	28	1.6	68.4
5	65	M	T2DM, HTN	5	189	88	94	1.2	150	80	YES	6.99	198	210	150	52	83	26	19	1.2	64.6
6	43	M	T2DM	2	175	78	89.3	1.1	110	80	NO	6.95	241	130	101	20	68	42	28	0.9	57.8
7	50	M	T2DM,HTN,CAD	4	191	77	99	1.1	140	80	YES	7.15	254.4	142	155	31	82	29	47	1.2	64.9
8	57	F	T2DM, HTN	3	182	74	87.8	1	140	90	YES	10.99	297	150	200	40	70	40	18	1.1	76.7
9	70	F	T2DM, HTN	5	173	65	89.1	1.2	130	90	YES	>14.0	192.7	141	171	71	34	37	20	0.9	65.8
10	48	M	T2DM	5	174	86	101.7	0.99	120	70	NO	10.64	291	104	130	26	50	28	23	0.8	78.2
11	38	M	T2DM	2	171	79	96.1	0.98	120	80	NO	9.34	121.2	156	260	52	74	30	78	1.1	79
12	55	F	T2DM	2	183	67	86.8	0.96	110	80	YES	7.57	198.2	119	205	41	45	33	65	0.78	75.6
13	65	F	T2DM, HTN	3	186	64	81	0.95	140	70	YES	8.9	72.3	109	150	30	60	19	109	0.4	103.9
14	76	M	T2DM,HTN	4	170	71	91.4	1.1	140	80	YES	6.8	247	130	101	20	68	42	28	1.8	74.7
15	70	F	T2DM	5	177	77	94	1.2	120	80	NO	9.01	258	142	155	31	82	29	47	1.2	78.3
16	36	M	T2DM	1	188	75	87	1.1	120	70	NO	6.89	65.61	110	95	19	52	39	28	1	77.1
17	55	F	T2DM,HTN	2	162	74	100	1	160	80	YES	13.1	171.5	173	525	70	98	33	77	1.1	69.7
18	40	F	T2DM	4	147	50	102	0.98	110	80	NO	>14.0	136	269	233	47	186	36	32	1.5	79.7
19	45	M	T2DM HTN	1	145	55	97	1	140	90	NO	13.01	65.6	155	134	27	98	31	24	0.7	86
20	45	F	T2DM	4	157	55	94	1.01	130	70	NO	12.72	285.5	94	227	45	40	9	78	0.6	73.5
21	45	F	T2DM, HTN , CAD	5	161	60	102	1.2	150	70	YES	6.9	290	165	311	62	61	42	31	0.5	64.2
22	44	M	HTN, T2DM	4	186	64	81	1.1	130	80	YES	10.68	238.5	142	155	19	52	39	24	1.8	59.5
23	52	M	T2DM	4	172	68	96	1.1	130	70	NO	6.54	139.9	119	391	78	26	14	29	0.9	89.7
24	64	F	T2DM,CAD, HTN, CVD	3	162	70	104	1	160	80	NO	6.5	252.1	195	147	29	106	59	87	1.7	88.1
25	50	F	T2DM	5	153	75	101	1.2	120	80	NO	9.2	94	231	99	20	151	60	64	1.3	64.1
26	45	F	T2DM	3	160	82	98	0.99	110	70	NO	9.95	278	150	136	27	89	34	19	0.9	57.9
27	50	F	T2DM, HTN	5	155	87	100	0.91	140	70	YES	12.2	270.7	163	278	51	102	21	42	0.8	47.1
28	42	M	T2DM,CVD	1	170	90	94	1	120	70	NO	8.95	72.8	181	134	27	98	31	25	0.8	69.2
29	38	M	T2DM	1	182	76	80	1.01	110	80	NO	7.11	141	162	51	44	72	30	42	1.7	75.1
30	42	F	T2DM	2	176	79	82	1.2	120	70	NO	7.95	198	109	104	24	64	46	29	0.8	61.4
31	50	M	T2DM, HTN	1	185	69	114	1.1	130	80	NO	6.56	240	182	161	38	82	31	47	0.7	78.6
32	52	F	T2DM,HTN	5	174	80	93	1.1	130	80	YES	7.2	92.8	199	93	58	88	57	60	0.3	79.2
33	45	F	T2DM,HTN,CAD	4	184	72	94	1	150	70	NO	6.5	140	200	78	66	72	43	48	2.1	61.3
34	65	M	T2DM,HTN,CAD	2	182	69	84	1.2	150	70	YES	6.65	218	197	236	59	56	33	35	0.9	94.1
35	45	M	T2DM, HTN	5	184	88	78	0.99	140	70	NO	11.11	198	85	152	29	42	44	47	0.8	65.2
36	32	M	T2DM	1	192	78	115	0.95	110	70	NO	11.44	258.1	126	262	17	76	44	67	1.1	83.5
37	63	M	T2DM,HTN	5	169	65	78	0.94	160	80	YES	10.48	242	134	156	50	64	28	20	1.2	58.3
38	75	M	T2DM, HTN	4	186	78	118	0.96	150	70	YES	6.78	282	91	149	18	72	54	30	1.1	58.9
39	65	M	T2DM	5	180	88	120	0.97	110	80	NO	7.84	194	222	329	62	82	37	35	0.7	88.9
40	45	M	T2DM, HTN	2	179	69	114	1	140	90	YES	9.38	200	146	192	72	69	56	53	0.5	80.5
41	50	F	T2DM,HTN	5	178	71	98	0.98	150	80	NO	11.29	132.4	130	225	43	118	47	76	0.9	61
42	63	M	T2DM	4	168	68	108	0.96	120	70	NO	10.07	241	155	356	72	92	62	238	0.7	69
43	56	F	T2DM	2	181	78	119	1	110	80	NO	6.75	198	166	301	72	84	42	182	0.8	68.2
44	59	M	T2DM, HTN	5	176	67	111	1.01	140	70	NO	6.99	263.5	93	103	39	26	33	27	0.8	78.5
45	55	F	T2DM,HTN	5	168	72	86	1.2	150	80	YES	11.75	82	103	320	57	88	42	67	1.5	89.5
46	58	F	T2DM	4	182	77	112	1.1	120	70	NO	6.9	204	92	263	86	38	103	103	0.7	78.2
47	55	M	T2DM, HTN	2	174	71	117	1.1	130	70	NO	7.78	273.2	164	222	44	76	55	17	1.1	76.8
48	55	M	T2DM	3	178	76	80	1	110	70	NO	7.9	94.9	198	208	24	62	40	59	1.9	87.2
49	55	M	T2DM, HTN	3	153	62	116	1.2	150	90	NO	12.54	212	143	252	21	16	25	21	1.9	85.2
50	32	F	T2DM,HTN	1	165	71	119	0.99	130	90	NO	7.85	116.1	147	276	32	54	31	63	0.9	91.4
51	61	F	T2DM,HTN	6	170	80	92	1.1	180	90	NO	8.2	252.1	180	199	36	70	28	118	3.7	57.3
52	45	M	T2DM	6	186	72	81.2	1.1	120	70	NO	12.72	139.9	210	150	52	83	26	19	1.4	74
53	55	M	T2DM, HTN	10	175	69	76.4	1	140	70	YES	11.6	224	193	127	50	145	42	29	1.2	74.9
54	56	M	T2DM,CAD	7	178	65	82.9	1.2	130	70	NO	8.05	201.1	105	60	12	42	52	51	1.5	60.8
55	65	M	T2DM, HTN	10	189	88	94	0.99	150	80	YES	6.99	198.2	210	150	52	83	26	19	1.2	75.3
56	50	M	T2DM,HTN,CAD	10	191	77	99	0.95	140	80	YES	7.15	251.4	142	155	31	82	29	47	1.2	76.1
57	57	F	T2DM, HTN	8	182	74	87.8	0.94	140	90	YES	10.99	129.7	150	200	40	70	40	18	1.1	81
58	70	F	T2DM, HTN	8	171	65	89.1	0.96	130	90	YES	>14.0	192.7	141	171	71	34	37	20	0.9	74.5
59	55	F	T2DM	8	183	67	86.8	0.97	110	80	YES	7.57	198.2	119	205	41	45	33	65	1.3	67.3
60	65	F	T2DM, HTN	10	186	64	81	1	140	70	YES	8.9	272.3	109	150	30	60	19	109	1.4	47.2
61	76	M	T2DM,HTN	6	170	71	91.4	1.1	140	80	YES	6.8	124.7	130	101	20	68	42	28	1.8	76
62	70	F	T2DM	8	177	77	94	1.1	120	80	NO	9.01	258.2	142	155	31	82	29	47	1.2	52.7
63	81	M	T2DM, HTN	9	184	73	80	1	150	80	NO	7.02	191.1	120	160	50	74	30	34	2.8	76.6
64	80	M	T2DM, HTN	10	194	80	92	1.2	130	70	NO	6.6	252.1	120	160	20	68	42	70	1.7	54.1
65	55	F	T2DM,HTN	10	162	74	100	0.99	160	80	YES	13.1	171.5	173	525	70	98	33	77	1.1	82.3
66	64	F	T2DM,CAD, HTN, CKD,CVD	6	162	70	104	0.95	160	80	NO	6.5	252.1	195	147	29	106	59	87	2.8	57.8
67	50	F	T2DM	8	153	75	101	0.94	120	80	NO	9.2	94	231	99	20	151	60	64	1.3	86
68	65	F	T2DM,HTN	9	165	90	102	1.1	150	80	YES	9.2	65.6	172	199	31	99	35	20	0.6	76.8
69	50	M	T2DM, HTN	10	185	69	114	1.1	130	80	NO	6.56	240.3	182	161	38	82	31	47	0.7	77.8
70	52	F	T2DM,HTN	8	174	80	93	1	130	80	YES	7.2	92.8	199	93	58	88	57	60	3.3	85.3
71	45	F	T2DM,HTN,CAD	7	184	72	94	1.2	150	70	NO	6.5	140.1	200	78	66	72	43	48	7.1	69
72	65	M	T2DM,HTN,CAD	6	182	69	84	0.99	150	70	YES	6.65	218.2	197	236	59	56	33	35	1.3	77.8
73	75	M	T2DM, HTN	7	186	78	118	0.95	150	70	YES	6.78	218.4	91	149	18	72	54	30	1.1	76.1
74	45	M	T2DM, HTN	8	179	69	114	0.94	140	90	YES	9.38	120	146	192	72	69	56	53	0.5	87.5
75	63	M	T2DM	10	168	68	108	0.96	120	70	NO	10.07	291.2	155	356	52	92	62	238	0.7	48.1
76	56	F	T2DM	8	181	78	119	0.97	130	80	NO	6.75	198	166	301	72	84	42	182	0.8	78.1
77	59	M	T2DM, HTN	10	176	67	111	1	140	70	NO	6.99	263.5	93	103	39	26	33	27	0.8	44.5
78	58	F	T2DM	8	182	77	112	0.98	120	70	NO	6.9	120.4	92	282	63	86	38	103	0.7	82.7
79	55	M	T2DM, HTN	10	174	71	117	0.95	130	70	NO	7.78	273.2	164	222	44	76	55	17	3.1	49.8
80	30	M	T2DM, HTN	8	188	84	118	1	130	70	NO	6.7	237.5	153	138	55	79	62	48	2.8	76.3
81	64	M	T2DM, HTN , CAD	9	192	88	116	1.01	150	80	NO	8.35	218.2	219	242	20	58	54	58	3.1	55.9
82	72	F	T2DM, HTN	9	181	72	90.1	1.2	150	70	NO	7.35	124.3	190	245	27	44	41	18	2.7	77.6
83	55	M	T2DM	6	178	76	80	1.1	110	70	NO	7.9	94.9	198	208	24	62	40	59	1.9	84
84	81	M	T2DM,HTN,CAD	9	193	82	118	0.98	130	90	YES	11.49	207.2	217	99	33	74	34	37	3	55.1
85	75	M	T2DM,HTN	9	168	78	115	0.96	150	80	NO	7.31	191.3	114	308	33	48	66	50	3	66
86	55	M	T2DM, HTN	8	151	62	116	0.94	150	90	NO	12.54	212	143	252	21	16	25	21	2.9	72.8
87	61	M	T2DM	9	177	65	129	0.97	110	70	NO	6.65	114.5	138	492	48	124	60	28	2	67.5
88	60	F	T2DM,HTN	8	167	78	123	0.95	160	80	NO	6.55	256.2	182	262	50	98	17	64	3	60
89	55	F	T2DM,CVD	10	180	84	119	0.99	120	70	NO	7.09	258.1	163	122	30	82	19	59	1.4	58.8
90	55	F	T2DM	7	172	74	118	1.1	120	80	NO	7.97	190.2	121	124	66	52	34	19	0.5	74.7
91	65	M	T2DM, HTN	7	175	77	105	1.1	150	90	YES	10.96	162	132	292	52	64	46	23	1	65
92	56	F	T2DM,CVD	6	183	72	124	1	110	80	NO	10.84	256	127	312	92	88	13	53	0.6	56.8
93	45	M	T2DM,HTN	9	181	81	102	1.2	150	90	NO	6.02	292	196	399	72	42	39	22	1.6	46.3
94	51	M	T2DM,CAD	7	173	74	124	0.99	120	80	NO	8.17	240.2	162	280	74	64	33	132	1	72.9
95	55	F	T2DM, HTN	7	180	75	114	0.95	140	80	YES	6.92	75.61	107	380	72	29	54	19	1.2	74.1
96	65	F	T2DM,HTN,CAD	7	181	72	91.2	0.94	160	80	YES	7.24	200	104	154	68	88	59	53	0.9	76
97	50	F	T2DM, HTN	8	181	73	86.8	0.96	140	80	NO	6.84	201	109	91	48	71	27	39	0.6	83.5
98	51	M	T2DM	7	172	76	81	0.97	120	70	NO	7.95	231	170	96	38	34	72	121	0.4	77.1
99	38	M	T2DM, HTN	8	181	65	94.5	1	140	70	YES	6.95	52.7	184	65	84	43	18	29	0.7	84.5
100	55	F	T2DM,HTN	10	174	68	90.1	0.98	140	90	YES	10.65	190	79	143	98	42	30	35	0.6	86.4
101	61	F	T2DM,HTN	25	170	80	92	0.98	180	90	NO	8.2	252.2	180	199	36	70	28	118	3.7	67.3
102	53	M	T2DM,HTN,CAD	18	166	75	89.3	0.96	150	70	NO	7.7	277	200	160	52	68	34	165	6	41
103	65	M	T2DM,HTN	18	180	77	89	0.95	130	90	NO	7.1	216.5	93	51	10	48	35	137	2.3	72.3
104	56	M	T2DM,CVD	17	178	65	82.9	1.1	130	70	NO	8.05	120.2	105	60	12	42	52	51	1.5	76.8
105	74	M	T2DM,HTN,CAD	21	186	76	82.4	1.2	140	80	NO	7.5	254.8	104	130	26	50	28	23	3.7	66.9
106	60	M	T2DM,HTN	16	170	80	99	0.98	130	90	YES	9.78	214.2	156	260	52	74	30	78	1.6	63.4
107	76	M	T2DM,HTN,CAD	14	180	68	79.4	0.96	160	90	NO	7.16	220.1	93	51	10	48	35	137	4.1	40.9
108	60	M	T2DM,HTN	12	170	69	79.6	0.95	150	70	NO	10.45	190.2	109	150	30	60	19	109	1.8	53.5
109	70	M	T2DM	12	180	78	91	1.1	110	80	NO	8.54	241.8	170	151	49	72	28	38	1	48
110	74	M	T2DM,HTN	20	180	72	91.2	0.98	140	90	NO	7.13	234.3	120	160	32	50	38	62	2.8	44
111	75	F	T2DM,HTN	15	183	69	80	0.96	150	90	YES	6.9	252.4	150	158	32	90	28	68	1.3	48
112	69	M	T2DM	12	182	70	89.1	0.95	120	70	NO	7.74	290	163	118	24	109	30	32	1.9	40
113	75	F	T2DM,CAD,CVD	22	191	81	94.5	1.1	130	70	NO	7	205.5	126	76	15	63	48	19	3.2	46.3
114	65	M	T2DM, HTN , CAD	15	190	85	90.1	1.2	130	80	YES	8.9	283.3	105	95	42	19	44	36	1.2	49
115	81	M	T2DM, HTN	19	184	73	80	1.1	150	80	NO	7.02	291.2	120	160	50	74	30	34	2.8	46
116	80	M	T2DM, HTN	30	194	80	92	1	130	70	NO	6.6	252.2	120	160	20	68	42	70	1.7	46
117	62	M	T2DM, HTN	12	170	85	98.3	0.95	140	70	YES	7.5	241.8	170	151	49	72	28	38	1.4	46
118	50	F	T2DM,HTN, CAD	15	164	80	101	0.98	140	90	NO	8.46	270.2	134	161	32	47	56	45	3.9	47
119	45	F	T2DM	13	160	82	98	0.96	110	70	NO	9.95	129.2	150	136	27	89	34	19	0.9	64.5
120	65	F	T2DM,HTN	19	165	90	102	0.95	150	80	YES	9.2	95.6	172	199	31	99	35	20	0.6	68
121	50	M	T2DM,CVD	12	172	81	89	1.1	130	80	NO	6.6	242.2	172	160	28	40	47	199	1.4	46
122	71	F	T2DM,CVD	26	183	70	98	1.2	150	70	NO	7.22	201	98	152	42	76	33	40	1.4	60.1
123	45	F	T2DM,HTN,CAD	17	184	72	94	1.1	150	70	NO	7.1	240.2	196	80	64	79	40	44	7.7	47
124	65	M	T2DM,HTN	16	174	81	87	1	150	70	YES	9.23	243.7	184	152	49	64	54	42	1.4	48
125	42	F	T2DM, HTN	15	173	79	86	1.1	130	80	NO	12.68	242.2	105	250	38	31	32	104	6.6	43.9
126	75	M	T2DM, HTN	17	186	78	118	1	130	70	YES	6.78	284.1	91	149	18	72	54	30	1.1	44
127	60	M	T2DM	13	174	91	117	1.01	110	80	YES	6.96	141	111	247	66	54	29	23	0.6	67.3
128	71	F	T2DM,HTN	15	185	64	116	0.98	140	90	YES	8.37	203	269	444	48	62	33	15	0.7	61
129	30	M	T2DM, HTN	25	188	84	118	0.96	130	70	NO	6.7	200.4	153	138	55	79	62	48	2.8	56.3
130	64	M	T2DM, HTN , CAD	11	192	88	116	0.95	150	80	NO	8.35	288	219	242	20	58	54	58	3.1	42
131	72	F	T2DM, HTN	19	181	72	90.1	1.1	150	70	NO	7.35	210.2	190	245	27	44	41	18	2.7	47.6
132	81	M	T2DM,HTN,CAD	30	193	82	118	1.2	130	90	NO	11.49	207.6	217	99	33	74	34	37	3	45.1
133	62	M	T2DM, HTN	12	173	82	124	0.98	140	90	NO	6.8	204	180	321	49	137	72	15	2.9	64
134	75	M	T2DM,HTN	25	168	78	115	0.96	150	80	NO	7.31	264.5	114	308	33	48	66	50	3	46
135	61	M	T2DM	15	177	65	129	0.98	110	70	NO	6.65	114.5	138	492	48	124	60	28	2	67.5
136	65	F	HTN, T2DM	12	183	65	114	0.96	150	70	NO	6.1	261.2	176	212	16	151	42	37	2.6	40
137	45	M	T2DM	13	169	81	124	0.95	150	70	NO	9.4	241.8	196	246	62	74	49	22	2.5	64.5
138	55	F	T2DM	17	172	74	118	1.1	120	80	NO	7.97	241.6	121	124	66	52	34	19	0.5	55
139	65	M	T2DM, HTN	17	175	77	105	1.2	150	90	YES	10.96	162.2	132	292	52	64	46	23	1.4	54
140	45	M	T2DM,HTN	19	181	81	102	0.98	150	90	NO	6.62	294.2	156	399	72	42	39	22	1.1	42
141	51	M	T2DM,CVD	14	173	74	124	0.96	120	80	NO	8.17	240.3	162	280	74	64	33	132	1	50
142	69	F	T2DM,HTN	12	175	69	119	0.95	180	70	NO	10.2	254.2	164	311	33	72	22	63	5.1	46
143	60	M	T2DM, STROKE	21	170	64	134	1.1	120	80	NO	6.79	239.5	122	160	46	32	16	50	2.1	54.2
144	55	F	T2DM, HTN	14	180	75	114	0.98	140	80	YES	6.92	207	107	351	72	32	49	20	1.1	54.9
145	65	F	T2DM,HTN,CAD	12	181	72	91.2	0.96	160	80	YES	7.24	202.6	104	154	68	88	59	53	0.9	66
146	75	M	T2DM,HTN	15	178	82	101.7	0.95	140	70	YES	7.02	96.8	105	164	46	72	17	22	0.9	78
147	51	M	T2DM	11	172	76	81	1.1	120	70	NO	7.95	204.6	170	96	38	34	72	121	0.4	67.1
148	73	M	T2DM,HTN,CAD	18	163	70	91.4	1.2	140	90	YES	11.02	291.1	172	214	20	48	20	170	1.2	45
149	72	F	T2DM,HTN	20	175	81	94	1.1	130	80	NO	12.98	57.2	148	57	64	65	14	19	0.5	59
150	52	F	T2DM	14	172	70	80	1	110	80	NO	8.28	290	172	254	23	66	16	17	1.4	48